VOLUME XXVI NUMBER 3

DISEASES

of the

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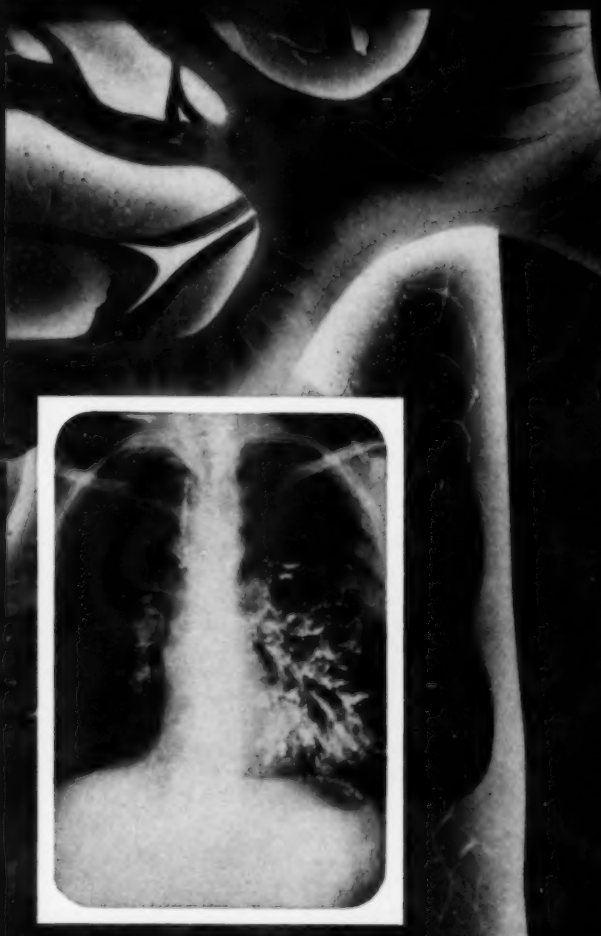

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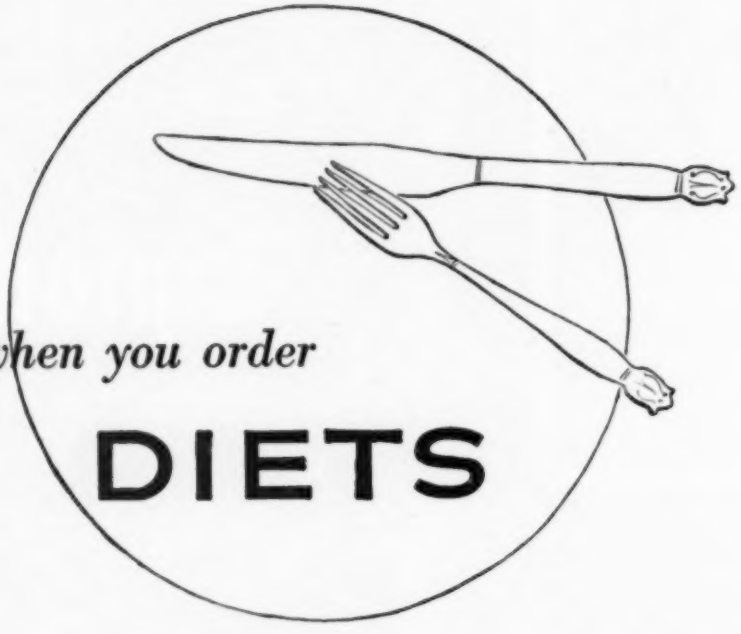

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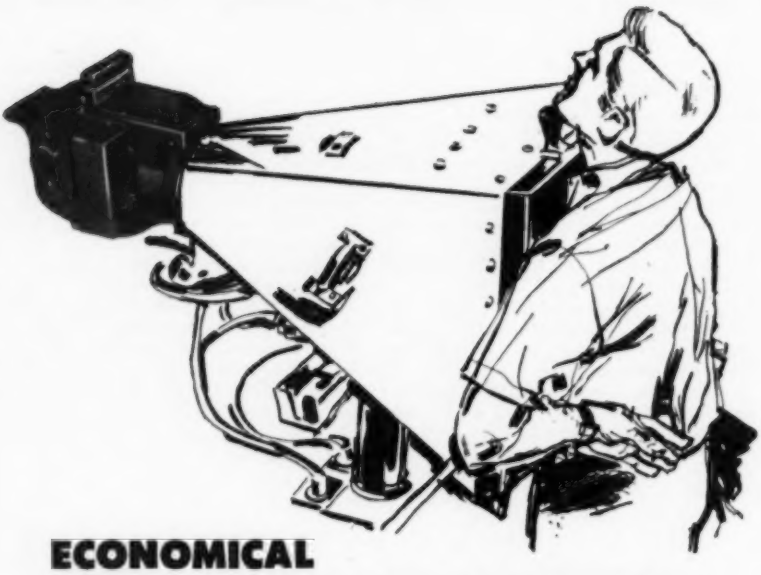

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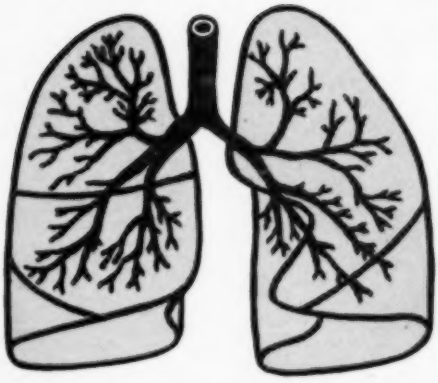

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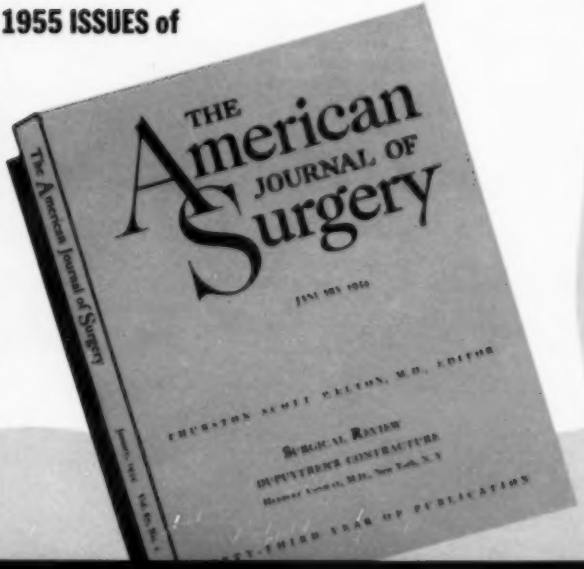

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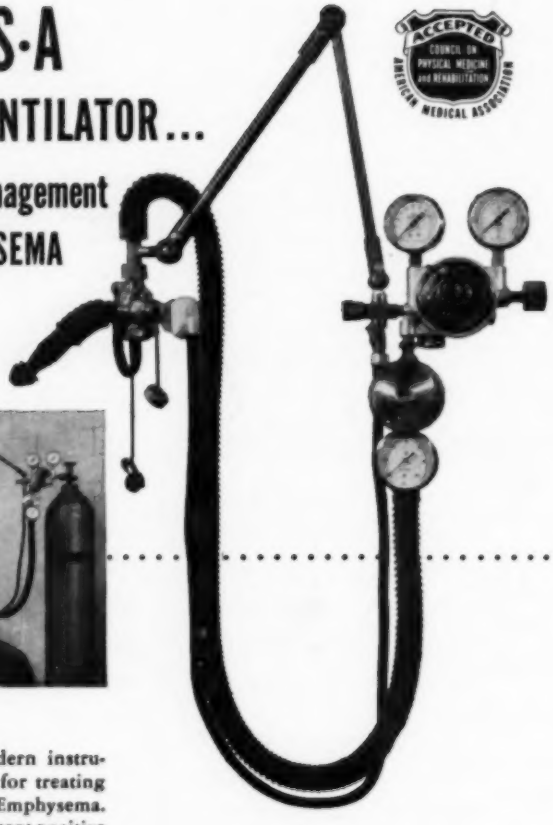

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1. Hobby, G. L., Lenert, T. F., Rivoire, Z. C., Donikian, M., and Pikula, D.: Am. Rev. Tubere. 67:808, 1953.

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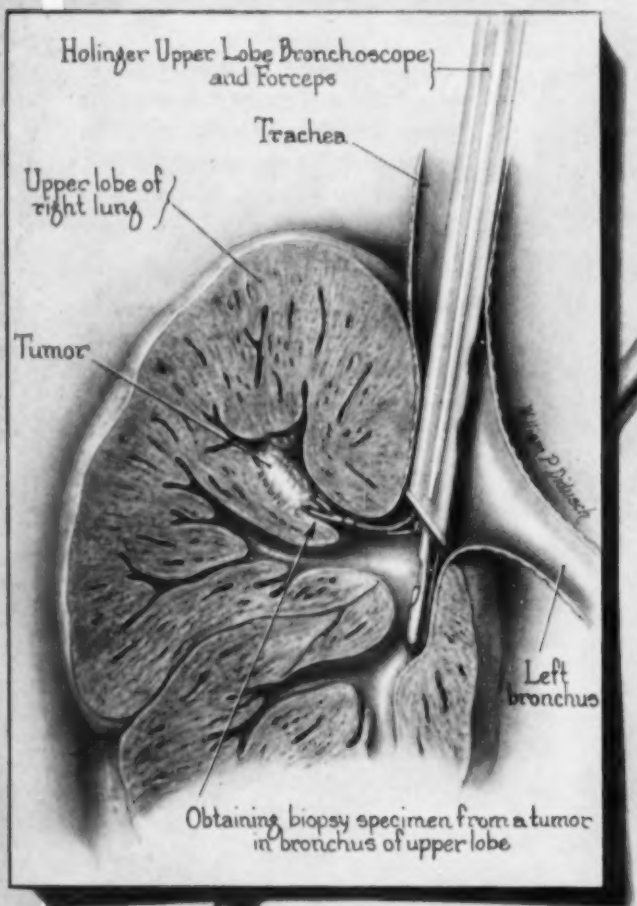
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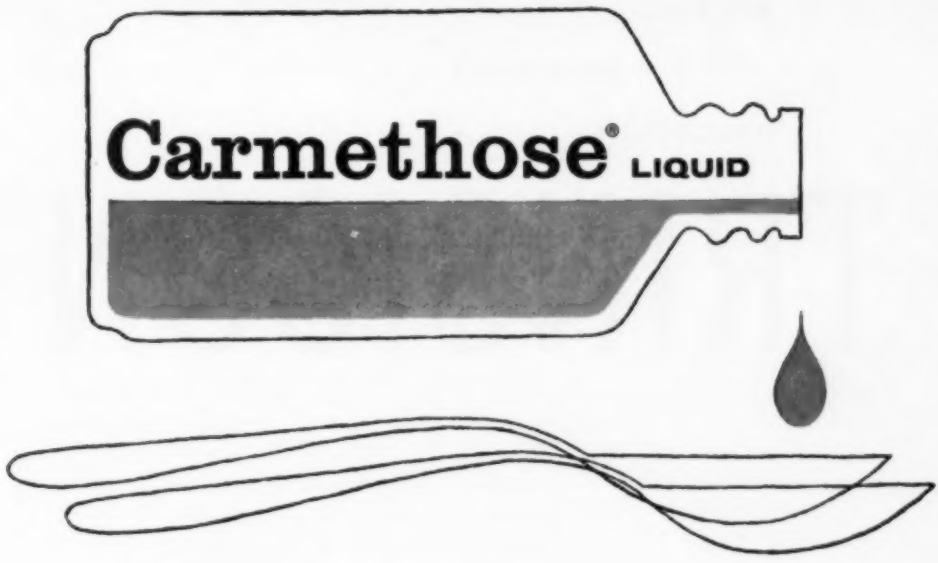

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DISEASES *of the* CHEST

VOLUME XXVI SEPTEMBER 1954 NUMBER 3

Roentgenologic Changes of the Lung Associated with Isoniazid Therapy in Pulmonary Tuberculosis*

DAVID SALKIN, M.D., F.C.C.P. and J. A. SCHWARTZ, M.D., F.C.C.P.
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The value of isoniazid as a therapeutic agent in pulmonary tuberculosis is well established but its roentgen effects have not been so well determined and need further clarification. Beneficial changes described by various authors include resorption of lesions, better definition (hardening), diminution of the extent and density of homogenous shadows, disappearance of post-hemorrhagic spreads, and decrease in size or closure of cavities or thinning of their walls.

Most of the published studies mention chiefly the general incidence of roentgen improvement and present great variation in results. For example, both the United States Public Health studies[1] and the Veterans Administration[2] report some degree of roentgen improvement in about 60 to 70 per cent of patients and moderate and marked degrees in 40 to 50 per cent. The British Medical Research Council[3] found moderate improvement in 20 per cent, Tanner[4] in 17 per cent, and Brun[5] and Maccone[6] found few noteworthy changes.

The time of appearance of the roentgen changes has been described as occurring early by some and late by others. It has also been noted that certain types of lesions respond better than do others. Good results were noted most often in fresh exudative lesions and poorest results in fibrotic lesions and old cavities.[6-8] The incidence of such improvement has been determined in only a small sporadic series of cases; for example, the British Research Council[3] reported improvement in 40 per cent of 51 cases of acute progressive disease, Witkind[9] found only one improvement in 12 cases of caseous pneumonia, and Collins[10] noted favorable changes chiefly in the exudative element of chronic cases. The improvement reported in cavities also varied markedly. Tchertkoff[11] reported a decrease in size in 53 per cent, with cavity closure in 30 per cent; Duggeli[12] reported improvement in 50 per cent; Collins[10] in 45 per cent of 11 cavernous cases and

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28 per cent of 18 fibroid cases; and Robitzek[13] in 39 per cent with closure in 14 per cent. It has also been noted that the emergence of bacterial resistance and the conversion of sputum often showed no corresponding roentgen changes. Wacker[7] noted favorable x-ray changes occurring after development of resistance and Tanner[4] described conversion of sputum even though the roentgenogram showed an increase of the disease.

The purpose of this study is to determine the incidence of roentgen improvement produced by isoniazid in the different types of infiltrations and cavities in 106 patients, the effect of certain factors, the time of occurrence of the changes, and the effect of resistance development.

Clinical Data

This group of patients presented the following features at the beginning of isoniazid therapy. The average age was 49 years and fully 20 per cent were over 60. The average duration of tuberculosis prior to treatment was over nine years. Positive sputum was present in 86 at the beginning of therapy and had been present in the others some months previously. Eighteen had not had streptomycin therapy, 42 had streptomycin in varying amounts and were still sensitive to 10 mcg., 28 showed full resistance to 10 mcg. The roentgen classification of the extent of the disease included far advanced disease in 85, moderately advanced in 19, and minimal in two. The 212 individual lungs showed far advanced disease in 108 lungs, moderately advanced in 66, minimal in 22, ar.d no disease in 16. Thoracoplasty was present in 10 patients and significant emphysema in 35. All but four were male and 96 were white.

Isoniazid was the only chemotherapeutic agent used and the *dosage* was 150 mg. daily to 73 patients, 300 mg. to 19, and a variable dose from 225 mg. to 400 mg. to 14. None was included unless he had a minimum of three months of continuous therapy. Thus, 31 had treatment for three to six months, 50 for seven to 12 months, and 25 for 12 to 15 months.

Treatment with isoniazid was begun in March 1952 and additional cases were added up to August 1952. This analysis of the results was made as of July 1953. Where the treatment was continued to this date, the period of observation coincided with the period of treatment as was the case with 69 patients; where the isoniazid was discontinued prior to this date, the observation was continued until July 1953, unless another therapeutic agent was added.

Mode of Evaluation

This study does not deal primarily with the number of patients who showed roentgen benefit but with the effect of isoniazid upon the various types of lesions presented by this group. Thus, one patient may show an old fibroid cavity, productive disease, a recent exudative infiltration, and a recent exudative cavity and all may react differently to isoniazid. Such a case was regarded as having four types of lesions classified according to the pathological characteristics of the various areas of disease.

The infiltrations were designated as inactive and active. The inactive

group included moderate sized areas of fibrosis which had shown no change for months and moderate sized areas of parenchymal calcification. The *active* group was subdivided into the classical exudative and productive lesions and, because we had frequent excellent roentgengrams, and extensive serial studies with a knowledge of the age of the infiltrates, we added two more classes; an exudative-productive group between the exudative and productive and a productive-fibroid group (fibro-productive) between the productive and true fibroid. In order of age, the classification consisted of exudative, exudative-productive, productive, productive-fibroid, and fibroid lesions. The *cavities* were similarly subdivided based upon the nature and age of the cavity, its wall, and the original associated disease.

The classifications were made at the end of the observation period and designated the status of the disease existing just prior to isoniazid therapy. No case was classified on a single roentgenogram but on a thorough knowledge of each case including series of roentgenograms encompassing not only the period of treatment but for months and years prior to treatment. This classification by hindsight was intentionally adopted to enable us to classify the pathological characteristics of the lesions as accurately as possible.

Following therapy, the infiltrations were classified as worse, no change, or improved; and, if improved, whether to a mild, moderate, marked, or excellent degree. The mild degrees of improvement implied definite though small beneficial change, whereas excellent improvement meant complete or almost complete clearing. The beneficial effects upon cavities were described as decrease in size, closure, or blocking.

Those for isoniazid therapy were selected by a system of randomization adopted by the Veterans Administration and based upon the last digit of the hospital registry number. In this study, 23 were new admissions to the hospital and 83 were hospital residents who had not done well on other therapies or who were improving too slowly.

No other tuberculostatic drug was given simultaneously and existing pneumotherapy was continued unchanged. The degree of rest was also unchanged and, except for a few acutely ill who were on strict bed rest, almost all were on a modified rest program which permitted bathroom privileges. In lesions showing previous progression or quiescence the effect of isoniazid was evaluated easily, but in lesions showing some improvement prior to isoniazid, evaluation was, of course, more difficult, and great conservatism was shown in ascribing additional benefits to the drug.

Infiltrations

The inactive infiltrations were unaffected roentgenologically by isoniazid. The 27 areas of fibrosis in 27 lungs, the 12 parenchymal areas of calcification, and the numerous calcifications in the lymph nodes showed no change in appearance.

The active infiltrations numbered 135 areas, with some improvement noted in 35 (25 per cent). The incidence of degree of improvement varied

with the type of lesion present (Table I), ranging from 64 per cent in exudative cases to 4 per cent in the productive-fibroid infiltrations.

Extent of disease had a definite bearing upon improvement. The exudative group showed 80 per cent improved in minimal cases, 70 per cent in moderately advanced, and 33 per cent in far advanced. The exudative-productive group showed 50 per cent improved in minimal, and 12 per cent in moderate cases. The productive-fibroid figures formed too small a number to analyze. In all categories, minimal cases responded best, moderately advanced somewhat less, and far advanced poorest.

TABLE I: ALL DEGREES OF IMPROVEMENT OCCURRING IN THE DIFFERENT TYPES OF LESIONS

	No. Areas	No. Improved	Per Cent Improved
Exudative	36	23	64
Exudative-productive	16	6	37
Productive	28	4	14
Productive-fibroid	55	2	4
TOTAL	135	35	25

The *initial time* of roentgen improvement occurred in one month to three months and only once did it occur later. Early changes after only one month were seen in 50 per cent of the exudative lesions. Improvement then continued for months, although the greatest change occurred within the first five months with a slower but steady improvement thereafter. The *degree* of improvement followed a definite pattern. Exudative areas showed a large number of excellent and marked degrees of improvement; exudative-productive cases showed fewer excellent and marked clearings; productive and productive-fibroid areas showed chiefly lower grades of improvement.

Streptomycin resistance proved to be a definite factor in all the groups. Cases showing organisms which were sensitive or partially resistant to 10 mcg. streptomycin gave equal results in their reactions to isoniazid and showed about four times as many improved areas as those fully resistant to 10 mcg. streptomycin.

Although the number of cases in each group is too small for detailed analysis, they all appeared similar in the presence of such concomitant factors as presence of cavity, presence of other infiltrations, and presence of isoniazid resistance. It is true that the streptomycin group of cases form a more difficult group to treat by any method, but this, in itself, did not explain the difference in results.

Two lesions in one patient tended to react similarly to isoniazid if both showed the same pathological characteristics. In a group of 10 patients showing exudative disease in both lungs, seven showed improvement bilaterally at about the same time and degree, and three presented no change on either side. New disease developed in 10 patients while under treatment. Regression of a hitherto improving lesion occurred in very few cases.

Cavities

There were 81 patients with 107 distinct cavities. Decrease in cavity size occurred in 25 (23 per cent), including closure of five. Their reaction according to the pathological characters is shown in Table II.

Exudative, exudative-productive, and productive-fibroid cavities showed some degree of improvement in 27, 20, and 22 per cent respectively. Only 7 per cent of the fibroid cavities showed decrease in size. Productive cavities presented a relatively high figure of 45 per cent, and, though the total numbers are small, there may have been additional bronchial disease which improved, resulting in favorable mechanical changes.

TABLE II
IMPROVEMENT OCCURRING IN THE DIFFERENT TYPES OF CAVITIES

	No. Cavities	No. Closed	No. Smaller	Total Improved (Per Cent)
Exudative	11	1	2	27
Exudative-productive	25	1	4	20
Productive	13	1	5	45
Productive-fibroid	44	2	8	22
Fibroid	14	0	1	7
TOTAL	107	5	20	23

Size of the cavity was not a great factor. Closed cavities averaged 3.6 cm. in diameter; the others showing a decrease in size were 5.1 cm. and the unimproved 4.5 cm. The entire group of cavities averaged 5 cm. in diameter and ranged from 3 cm. to 10 cm. The *initial* change occurred in the first three months, and half of the cavities showed some change within two months. The maximum change occurred in 50 per cent of cavities in three months, in 25 per cent more in three to six months, and in the remaining 25 per cent after six months. Sensitivity to 10 mcg. streptomycin appeared to be a factor, for improvement occurred in 28 per cent of the sensitive cases, in 21 per cent of the partially resistant (10 mcg.), and in 13 per cent of the fully resistant. The *degree* of improvement varied from closure in five cavities, a decrease of over 50 per cent in size in seven, of 25 to 50 per cent in seven, and of 10 to 25 per cent in six.

Three cavities became smaller and then returned to their former size in two to four months. Thinning of the wall occurred four times and made the cavity difficult to see; in three of these the cavity also became smaller. The causes of this change might include improvement of a bronchial infiltration resulting in aeration of the atelectatic portions of the cavity wall. Multiple cavities in the same patient tended to react similarly if they had similar pathological characteristics; this occurred in 18 of 21 cases with such multiple cavities.

Isoniazid Resistance Studies

Resistance studies were made at three levels; namely, 0.2, 1.0 and 5.0 mcg. per ml. of Lowenstein-Jensen medium. It was noted that the time of resistance development did not always occur in a clean linear pattern. There was often rapid development of resistance to all levels in a short time; one month the organisms showed partial resistance to 0.2 mcg. and the next month partial resistance to 1.0 and 5.0 mcg. simultaneously. Frequent overlapping of resistance levels was common, and partial resistance to 5 mcg. often occurred before full resistance to 1.0 mcg.

In general, however, partial resistance to 5 mcg. occurred in 20 per cent of patients at three months, in 60 per cent at six months, and in 70 per cent at eight months. For purposes of attempting a correlation between resistance development and roentgen changes, the following tabulation was made showing the general average range of resistance development in most of the cases (Table III). It is to be noted that full resistance to 5.0 mcg. occurs in about five to seven months.

TABLE III
AVERAGE RANGE OF RESISTANCE DEVELOPMENT

Mcg/ml	Partial Resistance	Full Resistance
0.2	2 - 3 mos.	2 - 4 mos.
1.0	2 - 4 "	3 - 5 "
5.0	3 - 5 "	5 - 7 "

Further correlating the roentgen changes and isoniazid resistance, the following table is highly informative (Table IV).

TABLE IV: CORRELATION OF ROENTGEN IMPROVEMENT AND INH RESISTANCE DEVELOPMENT

Improvement	Disease		Relation to INH Resistance
Initial Improvement	Cavity Infiltration	1 to 3 mos. 1 to 3 mos.	Corresponds to full resistance to 0.2 mcg. or partial to 1.0 mcg.
Peak of Rapid Improvement	Cavity Infiltration	75% in 6 mos. Peak at 5 mos.	Corresponds to full resistance to 5 mcg.
Continuation of Improvement	Cavity Infiltration	Slight Continues	Cavities show little change after the development of resistance to 5 mcg. but the infiltrations continue to improve.

From the roentgen standpoint the level of significant resistance appears to be 5.0 mcg, but how important that may be remains to be determined. Once infiltrations begin to improve they tend to do so even after resistance develops, but cavities usually do not. It is possible that, in the case of infiltrations, the benefit initiated by isoniazid is continued by natural factors. In the case of cavities, the initial action on the bronchi and the

disease in the wall apparently produces conditions favorable to intrapulmonary mechanical changes (intrinsic collapse), which local factors seem to exist for only about six months in most cases.

Miscellaneous Features

Atelectasis occurred in a lobe or major segment 18 times in 17 patients. Within three months' treatment with isoniazid, five areas showed an increased retraction, two mildly, and three moderately. One segment of an atelectatic lobe became aerated while the rest of the lobe showed further shrinkage. All the changes occurred in cases associated with productive disease, suggesting some action on diseased bronchi.

Blocked Cavities occurred six times prior to therapy and four blocked during therapy—no more than the usual incidence. The drug seemed to have no effect on the production of blocked cavities, or did it influence them once they formed. There were too few so-called air-filled tension cavities to evaluate properly.

The production of *sputum* was decreased in most of the patients and, in many cases, it was difficult to obtain positive bacteriological findings despite the presence of cavity and "active" infiltration. In six patients, the sputum and gastric examinations became negative and remained so, in spite of definite cavitation.

Symptomatic improvement was common, and several of the more common ones are shown in Table V.

TABLE V

PER CENT IMPROVEMENT OF SEVERAL SYMPTOMS

	All Degrees	Moderate or Marked Degree	Improvement Then Reversion
General Improvement	89	70	7
Less Sputum	77	64	7
Less Cough	78	60	8
Gain in Weight	76	57	4

About 80 per cent of patients who showed some degree of improvement symptomatically maintained it despite development of resistance to 5 mcg. isoniazid. Where symptoms did revert they did so within the six months corresponding to resistance development to 5 mcg. About 95 per cent of patients showing some roentgen improvement also showed symptomatic improvement, and about 60 per cent who showed no roentgen changes had some symptomatic benefit.

SUMMARY

1) A group of 106 patients was treated with isoniazid for a period of from three to 15 months and the roentgen effects were observed on the various types of lesions present.

2) There were 135 areas of active infiltrations divided according to their

pathological characteristics and classified as exudative, exudative-productive, productive, and productive-fibroid groups, with roentgen improvement in 65, 37, 14, and 4 per cent respectively. The greatest improvement occurred in the more recent exudative lesions, in those of minimal or moderate extent, and in the streptomycin sensitive cases. Conversely, the poorest results were obtained in the older productive and fibroid lesions, in those far advanced, and in the streptomycin resistant cases. Initial roentgen changes occurred within three months, improvement continued rapidly up to about five months and thereafter at a slower but still steady rate. Such inactive infiltrations as true fibrosis and calcification were not altered in any way.

3) The 107 cavities in 81 patients were classified similarly to the infiltrations. Some reduction in size occurred in 25 cavities (23 per cent), including five closures. The productive cavities showed some decrease in size in 45 per cent, the fibroid in 7 per cent, and the others averaged 22 per cent. Apart from the five closures, the average decrease in size was 35 per cent, and the great majority remained small. Here, too, the initial changes occurred within three months, reaching a maximum at six months for 75 per cent of the cavities. Closed cavities were smaller than the others, but those showing only a partial decrease averaged the same size as those not responding at all. Better results were obtained in those cases sensitive to streptomycin than in those resistant to it.

4) The significant point of isoniazid resistance appeared to be at 5 mcg. Both infiltrations and cavities began to show improvement and reached initial rapid peaks within six months, corresponding roughly to development of full resistance to 5 mcg. isoniazid. After this period the cavities continued to show improvement in only 25 per cent, while almost all the infiltrations continued to show further benefit. It seems that, in the case of infiltrations, the benefit initiated by isoniazid was continued by natural factors, whereas, in the case of cavities, the initial changes produced by the drug included local mechanical alterations which operated within the shorter period of six months.

5) Symptomatic improvement occurred in almost all of the patients showing roentgen improvement and in 60 per cent of those showing no x-ray change.

CONCLUSIONS

From the roentgen standpoint, isoniazid does not cure tuberculosis. Its use is attended with varying results ranging from excellent clearing in fresh, localized exudative infiltrations to poor results in fibrocavernous lesions. It should prove to be a valuable adjunct in the comprehensive treatment of the disease.

CONCLUSIONES

Desde el punto de vista radiológico, la isoniacida no cura la tuberculosis. Su uso corresponde a resultados variables desde la excelente limpieza en las localizaciones infiltrativas recientes, hasta los resultados deficientes en

las lesiones fibrocavernosas. Parecería ser valiosa en calidad de adyuvante en el tratamiento global de la enfermedad.

RESUME

Du point de vue radiologique, l'isoniazide no permet pas la guérison de la tuberculose. Les résultats obtenus par son utilisation sont variables. Ils vont de l'excellent nettoyage des infiltrations exsudatives récentes el localisées aux faibles modifications des lésions fibrocavitaires. Il s'agit donc d'un adjuvant estimable dans le traitement rationnel de la maladie.

REFERENCES

1 Mount, Frank W. and Ferebee, Shirley H.: "Control Study of Comparative Efficacy of Isoniazid, Streptomycin-Isoniazid and Streptomycin-Para-Aminosalicylic Acid in Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, 67:539, 1953.

2 From the Statistical Tables (pp. 59-71) Used in the Transactions of the Twelfth Conference on the Chemotherapy of Tuberculosis held at Atlanta, Georgia, February 1953, prepared and edited by the Veterans Administration, Washington, D. C.

3 Tuberculosis Chemotherapy Trials Committee of the Medical Research Council: "The Treatment of Pulmonary Tuberculosis with Isoniazid," *Br. Med. J.*, No. 4787:735, Oct. 4, 1952.

4 Tanner, E., Wanner, J., Wehrlin, H. and Ramer, Z.: "Rimifon in der Behandlung der Tuberkulose; erste Klinische Beobachtungen," *Schweiz, Zeit. f. Tuberk.*, 4:255, 1952.

5 Brun, J. and Viallier, J.: "Isoniazide et tuberculose," *Rev. lyonn, Med.*, 1/7 (265-270), 1952.

6 Maccone, V., Romaldi, A. and Torriani, S.: "Observations on the Clinical Results of Isonicotinic Acid Hydrazide Therapy in Pulmonary Tuberculosis," *Acta. Tuberc. Scand.*, 28:123, 1953.

7 Wacker, T. and Bonard, E. C.: "Notes sur l'isonicotinyl-hydrazide (INH)," Semaine d. hop. Paris (La Semaine Medicale), Sept. 18, 1952, p. 583.

8 Martischnig, K. M. and Ward, P. M.: "Isonicotinic Acid Hydrazide in Pulmonary Tuberculosis," *Tubercle*, 34:14, 1953.

9 Witkind, E. and Willner, I.: "Clinical Experiences with Isonicotinic Acid Hydrazide in Tuberculosis," *Dis. of Chest*, 23:16, 1953.

10 Collins, D. M. and Bowen, D. A. L.: "Isoniazid in the Treatment of Pulmonary Tuberculosis," *Tubercle*, 34:8, 1953.

11 Tchertkoff, I. D., Asisian, M. and Nenashev, P.: "Treatment of Advanced Caseous-Pneumonic Tuberculosis with Isonicotinic Acid Hydrazides," *Quart. Bull. Sea View Hosp.*, 14:49, 1953.

12 Duggeli, O. and Trendelenburg, F.: "The Use of INH in Pulmonary Tuberculosis," *Tubercle*, 34:2, 1953.

13 Robitzek, E. H., Selikoff, I. J., Mamlok, E. and Tendlau, A.: "Isoniazid and Its Isopropyl Derivatives in the Therapy of Tuberculosis in Humans," *Dis. of Chest*, 23:1, 1953.

Peripheral Neuritis Due to Hydrazide Derivatives*

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The antituberculous activity of isoniazid used alone or in combination with streptomycin or para-aminosalicylic acid (PAS) has been established.[1] One of the most favorable properties of isoniazid is the low incidence of significant toxicity resulting from its use when doses of 3 to 5 mg. per kilogram per day are administered. Some of the reactions reported include toxic psychosis, convulsions, dizziness, euphoria, increased sensitivity to sympathomimetic drugs, hyperreflexia, weakness of the legs, headache, ataxia, muscle tremors, tinnitus, disturbed vision, insomnia, drowsiness, urinary incontinence, polyuria, delay in initiation of micturition, constipation, dryness of the mouth, drug fever, variations in sexual activity, pruritis, skin rash, nausea, vomiting, exertional dyspnea and transitory edema.[2] Although this is a long list, toxic reactions are infrequent. The need for discontinuing the drug because of serious toxic reactions occurs in approximately 1 per cent of cases.[3] It is interesting to note the dominance of toxic effects referrable to the nervous system.

In our studies with isoniazid, as well as other hydrazides, we have used various dosage schedules in an attempt to evaluate therapeutic efficacy, roentgenographic response, incidence of sputum conversion, development of bacterial resistance and drug toxicity.

In the course of these studies we have observed 19 patients who have developed peripheral neuritis of varying degrees of severity. Isoniazid was administered to 15. Three received 200 mg. daily; and 11 received 400 mg. daily. These doses represent 2.5 mg. to 10 mg. per kilogram per day. Eleven of the 15 received more than 5 mg. per kilogram per day. This indicates a correlation between the size of the dose and the development of neuritis.

The isoniazid used was supplied by two manufacturers. Three patients received isoniazid alone. Nine of these 15 received 1 gram of streptomycin twice a week and 12 grams of PAS daily in addition to isoniazid. One gram of streptomycin twice a week and daily isoniazid was administered to three, one of whom had received intermittent streptomycin and daily PAS for one year.

Four were given N-isonicotinoyl-N-(hydroxypivalidene) hydrazide.[4] In two of them 400 mg. of this compound was given daily; in one 200 mg. was administered. The third had received intermittent streptomycin and daily PAS for one year at which time 400 mg. of N-isonicotinoyl-N-(hydroxypivalidene) hydrazide per day was added. These doses correspond to 4.3 mg.

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to 11 mg. per kilogram per day. Three out of the four received over 5 mg. per kilogram per day.

Symptoms were noted as early as two weeks after the institution of therapy but in most cases appeared after the second month (Table I)

TABLE I
ONSET OF SYMPTOMS AFTER BEGINNING HYDRAZIDE THERAPY

	2 Weeks	2 Months	6 Months	9 Months	Over 1 Year
Isoniazid	2	6	3	1	3
N-isonicotinoyl-N-(hydroxypivalidene) hydrazide	2	1		1	

indicating a lack of strict correlation between duration of treatment and the onset of neuritis. The most common complaints were numbness, tingling, burning sensation and pain in the extremities. Fourteen had hypesthesia which was most severe in the fingers and/or toes. As the distal interphalangeal joint area was reached there was a rather abrupt increase in sensory appreciation. The findings are tabulated in Table II.

TABLE II: INCIDENCE OF SYMPTOMS OF NEURITIS IN NINETEEN PATIENTS RECEIVING ISONIAZID THERAPY

Clinical Manifestations	Number of Patients
Diminished vibratory sense	3
Hyperesthesia (pin prick)	4
Muscle weakness	5
Hyporeflexia	5
Hyperreflexia	6
Pain	11
Hypesthesia	14
Paresthesia	15

Although the findings were bilateral and had a typical "stocking and glove" distribution, in one patient there appeared to be a mononeuritis strictly limited to the distribution of the median nerve. In six the involvement was confined to the hands or was more severe in the hands, which is unusual for most types of peripheral neuritis. No changes were noted in skin color or temperature. Discontinuance of the responsible hydrazide usually resulted in improvement.

The pathogenesis of isoniazid peripheral neuritis is not known. One possible explanation is the interference with carbohydrate oxidation in nerve cell metabolism. In the oxidation of carbohydrate, nicotinic acid plays an important role as an essential consituent of co-enzyme I and II. One of the many reactions in which co-enzyme I participates is the conversion of pyruvic acid to lactic acid. It is possible that isoniazid with its similar structure might compete with nicotinic acid in this oxidative process thus producing a blocking mechanism. However, there was no

significant elevation of pyruvic acid levels in our patients.[5] Nicotinic acid also plays a role in the Kreb Cycle as co-enzyme activator for alpha-ketoglutarate dehydrogenase. Measures will be taken to determine if there is any increase in the alpha-ketoglutarate acids.

Although none of the patients showed any of the classical manifestations of nicotinic acid deficiency, the theoretical possibility exists that nicotinic acid may be useful in the management of isoniazid peripheral neuritis. It is our intention to use large doses of nicotinic acid in the patients who do not respond satisfactorily to the withdrawal of isoniazid.

Case Report

B. F., a 22-year-old colored female was admitted to this hospital on March 23, 1953, with a history of anorexia, weakness, and productive cough of several weeks' duration. X-ray film revealed evidence of extensive pulmonary disease. The sputum showed tubercle bacilli. Streptomycin, PAS and isoniazid were started on March 23, 1953. By April 20, 1953, there was obvious clinical and roentgenographic improvement. Two weeks after treatment was started, she complained of numbness and pain in both hands. The pain rapidly became worse and she described this "as if my flesh were coming off." Neurological examination revealed paresthesias of the hands, hyperactive reflexes, and greatly diminished pin-point sensation of both hands. Vibratory sense and position sense were intact. Gradually there was voluntary limitation of movement of both hands and fingers. Three weeks after the onset of symptoms there was considerable atrophy of the intrinsic muscles of the hands, particularly the thenar eminences, with almost complete loss of movement. On June 30, 1953, isoniazid was stopped. The peripheral neuritis continued for another month and then gradually subsided.

SUMMARY

Peripheral neuritis following isoniazid has been observed in 19 patients. The chief components are paresthesias of both upper and lower extremities. There was no strict correlation between duration of therapy and onset and severity of symptoms. In most instances symptoms gradually subsided following cessation of the drug.

RESUMEN

Se ha observado neuritis periférica en 19 enfermos después del uso de la isoniacida. Los principales síntomas son parestesias en ambas extremidades inferiores. No hay estricta correlación entre la duración del tratamiento y el principio y la severidad de los síntomas. En la mayoría de los casos los síntomas ceden después de la suspensión de la droga.

RESUME

Des études du système nerveux périphérique ont été faites après un traitement à l'isoniazide chez 19 malades. Les éléments essentiels des troubles sont des parestésies des extrémités. On ne peut noter de rapport net entre la gravité des manifestations et la longueur du traitement. Dans la plupart des cas, les signes pathologiques s'atténuèrent progressivement après qu'on eût cessé l'utilisation du produit.

REFERENCES

1 (a) Selikoff, I. J., Robitzek, E. H. and Ornstein, G. G.: "Treatment of Pulmonary Tuberculosis with Hydrazide Derivatives of Isonicotinic Acid," *J.A.M.A.*, 150:973, 1952.
(b) Clark, C. M., Elmendorf, D. F., Cawthon, W. U., Muschenheim, C. and McDermott, W.: "Isoniazid (Isonicotinic Acid Hydrazide) in the Treatment of Miliary and Meningeal Tuberculosis," *Am. Rev. Tuberc.*, 66:391, 1952.
(c) Tempel, C. W.: "Present Status of Specific Drug Treatment of Tuberculosis," *J.A.M.A.*, 150:1165, 1952.
(d) Pitts, F. W., Miller, F. L., Dye, W. E., Tempel, C. W. and FitzPatrick, M. J.: "Isoniazid Therapy in Pulmonary Tuberculosis. A Preliminary Report," *U. S. Armed Forces Med. J.*, 4:1, 1953.
(e) Selikoff, I. J. and Robitzek, E. H.: "Tuberculosis Chemotherapy with Hydrazine Derivatives of Isonicotinic Acid," *Dis. of Chest*, 21:385, 1952.
(f) Robitzek, E. H. and Selikoff, I. J.: "Isoniazid and Its Isopropyl Derivatives in the Therapy of Tuberculosis in Humans," *Dis. of Chest*, 23:1, 1953.
(g) Tempel, C. W., Pitts, F. W., Miller, F. L., Sands, J. H., FitzPatrick, M. J. and Weiser, O.: "Isoniazid-Streptomycin in the Treatment of Pulmonary Tuberculosis," Transactions of the Twelfth Conference on the Chemotherapy of Tuberculosis, Veterans Administration, Army and Navy, Atlanta, Ga., 1953, pp. 80-88.
(h) Katz, S., McCormick, G., Storey, P., Romansky, M. and Marshall, E.: "Isoniazid and Streptomycin Plus Isoniazid in the Management of Acute Tuberculous Pneumonia," Transactions of the Twelfth Conference on the Chemotherapy of Tuberculosis, Veterans Administration, Army and Navy, Atlanta, Ga., 1953, pp. 90-92.
2 References 1a, 1e, 1f and 1g.
3 Carr, D.: Transactions of the Twelfth Conference on the Chemotherapy of Tuberculosis, Veterans Administration, Army and Navy, Atlanta, Ga., 1953, p. 143.
4 Supplied by Dr. George Mast, Nepera Chemical Company, Yonkers, New York.
5 Pyruvic Acid levels performed through the courtesy of Dr. Joseph Fazekas, Chief of Staff, District of Columbia General Hospital.

Since the preparation of this report several references to isoniazid peripheral neuritis have appeared:

1 Gammon, G. D., Burge, F. W. and King, G.: "Neural Toxicity in Tuberculous Patients Treated with Isoniazid," *Arch. Neurol. and Psych.*, 70:64, 1953.
2 Quarterly Progress Report of the Veterans Administration. Army, Navy Study on the Chemotherapy of Tuberculosis, July 1953, pp. 44, 49, 51.
3 Biehl, J. P. and Skavlem, J.: Correspondence on Toxicity of Isoniazid, *Am. Rev. Tuberc.*, 68:296, 1953.

Results of the Use of Hydrazide of Isonicotinic Acid in the Therapy of Pulmonary Tuberculosis, Tuberculous Meningitis and Empyemas*

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PULMONARY TUBERCULOSIS

Material: Number of patients: 144. Type of disease: productive—exudative, mostly cavitary. Form: chronic. Daily dosage of INH: 4-10 mg./Kg. Duration of treatment: three to six months.

Results:

Clinically:

Pronounced improvement in 6 cases
Great improvement in 54 cases
Little improvement in 63 cases
No improvement in 19 cases
Deterioration in 2 cases } Death in 6 cases

X-ray Changes:

Great improvement in 14 cases (in 6 cases disappearance of cavities)
Little improvement in 46 cases
No change in 82 cases
Deterioration in 2 cases

Sputum Bacteriology:

123 patients had positive sputum for acid fast bacilli. In 41 the sputum was converted to negative. In 82 the sputum remained positive, and in 21 who had negative sputum, it remained negative.

Relapse:

After initial improvement 16 patients relapsed five months after beginning of treatment despite uninterrupted therapy.

Generally:

Favorable effect on the symptoms of the disease in high percentage; on the focal process moderate effect and in small percentage.

TUBERCULOUS MENINGITIS

1) Simple tuberculous meningitis treated by oral administration of hydrazide of isonicotinic acid alone.

Number of patients: 10.

Daily Dosage:

5- 10 mg./Kg. in two cases
10 mg./Kg. in eight cases

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Total Dosage:
40- 60 Gm. in four cases
60-100 Gm. in three cases
100-150 Gm. in three cases
Results:
Great clinical improvement without morbid signs and symptoms in two cases. Complete clinical and laboratory recovery in eight cases With duration of this favorable obtained result:
from two months in one case; three months in five cases;
four to five months in two cases.
Insufficient control time of stability and duration of the above mentioned eight cases.

2) Simple tuberculous meningitis previously treated with streptomycin and PAS without benefit and later treated with INH.
Number of patients: 15.
Total amount of streptomycin given intramuscularly from 70 to 220 Gm.; intraspinally 4.5 to 11 Gm.
Total amount of PAS: in eight cases from 600 to 2,200 Gm. intravenously.
Daily dosage of INH:
from 5-10 mg./Kg. in 10 cases
5 mg./Kg. in five cases
Total dose of INH:
from 35-50 Gm. in three cases
50-70 Gm. in six cases
70-95 Gm. in six cases
Results:
In one case, death. In six cases only clinical recovery with abnormal spinal fluid findings. In eight cases complete clinical and laboratory recovery.
Duration of clinical and laboratory recovery:
In one case, two months; one case, three months; one case, four months; one case, five months; four cases, six months.

3) Meningitis associated with pulmonary tuberculosis.
Number of patients: 23. Treated previously with streptomycin from 50 to 270 Gm. intramuscularly and 3 to 11 Gm. intrathecally, and PAS intravenously (in eight cases) from 400 to 2,200 Gm. Patients have failed to respond to this form of therapy and so INH treatment was started.
Daily dosage of INH:
5-10 mg./Kg. in 20 cases
10 mg./Kg. in three cases
Total dose of INH:
25-130 Gm. orally
Results:
Death in two cases

Deterioration in one case
No change in three cases
Improvement in six cases
Clinical and laboratory recovery in 11 cases

Duration of recovery:

Two months in two cases; three months in three cases; four months in two cases; five months in one case; six months in three cases.

On a total number of 48 patients of above three groups the following results were obtained:

Death in three cases
Deterioration in one case
No change in three cases
Improvement in 14 cases
Complete clinical and laboratory recovery in 27 cases.

EMPYEMATA

Number of cases: 18.

Treated previously by repeated aspiration and intrapleural administration of streptomycin and PAS and solution of hydrazide of isonicotinic acid unsuccessfully.

In 11 cases of tuberculous empyemas without bronchopleural fistulae, occurring as a complication of artificial pneumothorax, INH was given orally in daily dosage of 5 mg./Kg. for two to four months.

Results: Absorption of pleural effusion in all cases; in five cases enabling the pneumothorax to be continued. In six cases complete re-expansion of the collapsed lung with pleural obliteration was achieved.

In seven cases of tuberculous empyema with bronchopleural fistulae, in three as a result of artificial pneumothorax and in four as a complication of spontaneous pneumothorax, drainage was carried out.

INH therapy was instituted 10 mg./Kg. daily for five to eight months.

Results: Complete absorption of purulent effusion in four with re-expansion of the collapsed lung. Diminution of exudation in three. Closure of chest sinuses, healing of chest wall infection.

Observations and Conclusions

1) As regards the toxicity administration of daily dose of 10 mg./Kg. for months has not provoked undesirable side effects except some slight psychic disturbances. For example, a man, aged 38, suffering from meningitis and treated with hydrazide of isonicotinic acid and presenting great improvement tried to commit suicide by taking 80 tablets of INH (50 mg. per tablet). One hour later he vomited so that part of the tablets were expelled. Besides the acute toxic symptoms he presented hemiplegia which is improving, with residual paresia and a marked state of euphoria. A woman aged 27, suffering from pulmonary tuberculosis and treated with streptomycin, PAS and INH took by mistake 24 tablets of INH (50 mg. per tablet) daily for five days with resulting intense dizziness, headache and somnolence; after discontinuance of administration of the drug for three

days the symptoms disappeared to reappear again after a new course of 18 tablets daily for four days. Cessation of treatment: disappearance of toxic symptoms. Despite having taken in a period of 12 days, 192 tablets= 9 Gm. and 600 mg. of INH, toxic symptoms were observed but were transient without any sequelae.

2) Effect on pulmonary tuberculosis. Favorable effect on toxic symptoms was noted. The more acute and intense the morbid manifestations the greater the favorable effect. The milder the morbid manifestations the lesser the favorable effect. The more recent the focal process the greater the favorable effect. The older the focal process the lesser the favorable effect. In a small percentage of cases pronounced favorable results were observed. In a high percentage, life of patients was prolonged without morbid symptoms but without change in the focal process.

3) Effect on tuberculous meningitis, selective favorable influence with high percentage of complete clinical and laboratory recovery (27 out of 48 cases) was recorded. This selectivity is explained by the fact that the orally administered INH has a great penetrating and diffusion power in a high concentration rate in the spinal fluid as was determined by the researches of Bunger, Lass, Muller (Deut. Med. Wochenschrift, 19.IX.52, No. 38). In addition no hydrocephalus was observed in our cases owing to the fact that INH is administered orally and not intrathecally whereas the administration of streptomycin intraspinally favors the appearance of hydrocephalus, which aggravates the course and prognosis of meningitis as the necropsy researches of Zollinger,[1] Schwartz,[2] and Eleutheriou[3] have proved.

4) Selective favorable effect was noted with healing of tuberculous empyemas and of fistulae of empyemas by oral use of hydrazide of isonicotinic acid and not by local application of the drug. However, repeated aspiration and evacuation of effusion should be carried out during treatment.

The administration of larger daily dosage of INH is indicated as 10 mg./Kg. and not the initial proposed dose of 4 to 5 mg./Kg. As regards to the duration of administration of this agent we obtained favorable results by administration of this drug up to six months.

Further investigations are needed in order to solve the problem of the drug resistant strains. The published report of the British Medical Council of scientific researches (Brit. Med. Journal, X, 1952) mentions that by use of hydrazide of isonicotinic acid Koch bacilli show a resistance in 11 per cent at the end of the first month, 52 per cent at the end of the second month, and 71 per cent at the end of the third month.

Another question is the possibility of a synergistic action of hydrazide of isonicotinic acid with some other therapeutic agents such as streptomycin and PAS in order to obtain on the one hand more favorable results and on the other hand to decrease and delay the emergence of bacillary resistance to the combined administered drugs.

We consider INH a drug of attack so that by achievement of favorable

clinical results we may continue later with the combined treatment of streptomycin and PAS.

SUMMARY

The hydrazide of isonicotinic acid was administered to 144 persons with pulmonary tuberculosis, 48 with meningitis and 18 with empyema.

In doses of 10 milligrams per kilo of body weight, the only undesirable side effect were slight psychic disturbances.

Favorable effects were observed on toxic symptoms of pulmonary tuberculosis and in a large percentage, life was prolonged, but no change was observed in the lesions themselves.

Complete clinical and laboratory recovery occurred in 27 of the 48 cases of meningitis.

Selective favorable effect was noted with healing of tuberculous empyema and of fistulae by oral use of the drug.

RESUMEN

Se administró la hidracida del ácido isonicotínico a 144 personas con tuberculosis pulmonar (48 con meningitis y 18 con empiema).

A la dosis de 10 miligramos por kilo de peso, los únicos efectos indeseables parecen ser ligeros trastornos intestinales.

Se observaron efectos favorables sobre los síntomas tóxicos de la tuberculosis pulmonar y en gran porcentaje, la vida se prolongó, pero no se observó cambio en las lesiones mismas.

Se obtuvo una completa recuperación clínica y según el laboratorio de 27 entre 48 casos de meningitis.

Se notó efecto selectivo en la curación del empiema tuberculoso y de las fístulas mediante la administración oral de la droga.

RESUME

144 personnes atteintes de tuberculose pulmonaire (48 cas avec méningite et 18 cas avec pleurésie purulent) ont subi un traitement par l'isoniazide.

En utilisant les doses de 10 mmgr. par kilogramme de poids corporel, les seuls inconvénients furent de légers troubles.

On observa des effets heureux sur les signes d'intoxication de la tuberculose pulmonaire, et dans un nmbre important de cas, il y eut une prolongation de la durée de la vie. Mais l'auteur ne constata pas de modifications des lésions elles-mêmes.

Une guérison complète clinique et biologique, survint dans 27 des 48 cas de méningite.

On constata quelques effets favorables sur les pleurésies purulentes et sur les fistules en utilisant le produit par voie buccale.

REFERENCES

1 Zollinger, H., in Fanconi and Loffler: "Streptomycin and Tuberculosis," Basel, 1948.

2 Schwartz: *Schweitz. Zeitschr. f. Tuberkulose*, 1952, Zürich.

3 Eleutheriou, D.: "Tuberculosis of Childhood and Streptomycin—A Pathological Study," Reported at the Streptomycin Meeting, Paris, February 9-12, 1950.

Management of Spontaneous Pneumothorax*

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Spontaneous pneumothorax occurring in the apparently healthy individual was first named and described by Itard[1] in 1803. In 1826 Laennec[2] accurately described the occurrence of such a phenomenum, and following McDowell[3] in 1856, who described the condition in a tuberculous patient, the etiology was accepted as tuberculous in the majority of cases until Kjaergaard[4] (1932 and 1933) revealed that patients with spontaneous pneumothorax had no more tuberculosis than could be found in the general population. Leggett et al[5] (1934) found negative Mantoux tests in 50 per cent of their cases. Evidence of this basic pathological fact was furthered by Blackford[6] in 1939.

In a review of the literature on this subject, the monumental work by Kjaergaard,[4] the experimental work by Macklin,[7,8] and the clinical observations of Hamman[9] are easily outstanding. To those interested in the history of our knowledge of this subject from the earliest times up to 1903, we suggest the study of Emerson's monograph.[10]

Many names have been suggested and used to describe the non-tuberculous, non-traumatic pneumothorax in apparently healthy individuals. Spontaneous pneumothorax is by far the most commonly used; yet it infers that this type of pneumothorax occurs without known cause. From the work of the above,[4,7-9] as well as the operative findings and autopsy reports of others,[11-17] the etiology and pathogenesis is now well established, and perhaps a more descriptive term might be devised. None of the terms as listed in the literature are based on etiology or pathogenesis. Any terms which we have tried to devise that would have such a basis are quite clumsy, and we suggest return to the term first suggested by Kjaergaard[4] in 1933, to wit: "Pneumothorax simplex."

In the period 1949 to 1952 we have observed and treated 114 patients with spontaneous pneumothorax. Cases due to tuberculosis or other disease or trauma of any type, accidental or surgical, have been excluded from this series.

Source of Material

This material came from Medical and Surgical Chest Conferences at Brooke Army Hospital, Fort Sam Houston, Texas, from the Thoracic Surgery Center, Randolph Air Force Base, Texas, and from private cases.

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Age

The average age was 27.5 years. The youngest was a newborn infant, two months premature, and the oldest was 73 years. Fifty per cent of the total cases were under 25 years of age, and 80 per cent were under 30 years of age.

Sex

Male	104	patients
Female	10	"
TOTAL	114	

Types of Spontaneous Pneumothorax

Pneumothorax — First attack	61	
Pneumothorax — Recurrent attacks	47	
Hemopneumothorax	6	
TOTAL PATIENTS		114

Early in the first part of the series (1949), bronchoscopy and bronchography was done in 25 consecutive cases of initial attacks after expansion of the lungs. There were no positive findings on bronchoscopy, and the bronchograms were all negative. This procedure was then discontinued as a routine practice, being done thereafter only as indicated by symptoms or appearance of the lung after expansion.

Treatment of Unilateral Spontaneous Pneumothorax—First Attack

Bed rest only	10	
Thoracentesis only	12	
Intercostal catheter decompression	12	
Thoracoscopy with catheter decompression	12	
Thoracoscopy with instillation of glucose and catheter decompression	8	
Thoracoscopy with insufflation of talc and catheter decompression	5	
Thoracotomy with removal of large bullae and poudrage	1	
Decortication	1	
TOTAL PATIENTS		61

In 10 of the 61 patients, the degree of pneumothorax was quite small and no treatment was given but bed rest. We felt that the pneumothorax was so small that thoracentesis or insertion of an intercostal catheter might be injurious. In 12 cases thoracentesis alone (for the removal of air) was done. In the total 22 cases treated by bed rest only or bed rest and thoracentesis, there are four known recurrences.

In 12 cases treatment consisted of insertion of an intercostal catheter into the pleural space and decompression through a water trap. In 12 cases the catheter decompression was preceded by thoracoscopy. In these 24 cases there have been two known recurrences.

In eight cases thoracoscopy had been followed by instillation of 50 cc. of 50 per cent glucose into the pleural cavity, followed by catheter decompression. There has been one known recurrence.

In five cases during thoracoscopy talc (talcum powder, U.S.P.) was insufflated. There are no known recurrences.

In a total of 37 cases the intercostal catheter decompression was used. In the 22 cases treated by bed rest alone or bed rest and thoracentesis, an average of three weeks was required for complete expansion. The shortest time was eight days and the longest six weeks. Of the 37 in which intercostal catheter decompression was used, 33 were expanded within a few minutes following catheter insertion. Two of the remaining four were expanded by the second day, and the remaining two required six and eight days, respectively.

In one case, even though it was the first attack, the presence of a large bulla evident in the collapsed lung by roentgenogram led us primarily to a thoracotomy with removal of the bulla and poudrage. There has been no recurrence in this case.

In the last case in this group, an unexpanded lung developed as a sterile fibrothorax from the initial spontaneous pneumothorax. This patient had received elsewhere treatment in the following order: Bed rest for two weeks, repeated thoracenteses for three weeks, catheter decompression for two weeks. It is of interest to note that active treatment (thoracentesis) was delayed for two weeks, and continuous active treatment (intercostal catheter decompression) was delayed for five weeks. Decortication was necessary. There has been no recurrence.

In the early part of the series (1949), thoracoscopy was done in 25 cases (Curti and Poulsen[18]). In only two instances were blebs noted that could not be demonstrated on roentgenogram. For that reason it was discontinued as relatively useless. In the instances where thoracoscopy was done, a catheter was installed for decompression in all cases and instillation of glucose (eight cases) or insufflation of talc (five cases) was done. There were no complications or recurrences from the talc or glucose treated cases. The use of 50 cc. of 50 per cent glucose was discontinued because of pain. Intravenous procaine drip, intravenous morphine, and even the mixture of pontocaine with the glucose failed to reduce the pain to a reasonable degree. Pain was severe in six cases and moderately severe in two. The pain did not abate until an average of 72 hours had elapsed. Insufflation of talc was discontinued for the reason that it was difficult through the thoracoscopy trocars to place the talc exactly where desired. Too frequently it got into the interlobar fissures, mediastinal surface of the lobes, and the diaphragmatic surface of the lower lobe. These places, we feel, are undesirable in the use of talc.

Recurrent Spontaneous and Chronic Pneumothorax

Unilateral	28
Unilateral chronic unexpanded lung	6
Bilateral: Alternating	11
Bilateral: Simultaneous	2
TOTAL PATIENTS	47

Treatment of 34 Unilateral Recurrent and Chronic Spontaneous Pneumothoraces

Thoracotomy with resection of blebs, poudrage, and catheter decompression	18
Decortication with removal of blebs and catheter decompression	6
Catheter decompression	4
Thoracoscopy with instillation of glucose and catheter decompression	2
Phrenic emphraxis	1
Refused treatment	3
TOTAL PATIENTS	34

In the 18 cases operated, blebs or bullae were found in all but one. They were removed by excision, suturing the base, and inversion of this line of sutures by a secondary line of sutures. Poudrage was done by talc followed by catheter decompression. In the last four cases the pleura was also rubbed by gauze (Churchill[19]) previous to dusting by the talc. In the case wherein blebs were not found, rubbing and dusting with talc alone was done.

In the six cases of unexpanded chronic pneumothorax, it is of interest to note that four of the six developed the condition on their first recurrence. All required decortication of the thick fibroplastic peel. In all but one, upon expansion of the lung blebs or bullae were noted which were removed.

The four cases of catheter decompression, one of phrenic emphraxis, and two of instillation of glucose were all done in patients with marked bilateral emphysema, heart disease, considerable age, or a combination of all three.

There have been no recurrences in the 24 cases subjected to thoracotomy. One of the four treated by catheter decompression had a recurrence six months later, and two of the three refusing treatment had recurrences within the year.

Bilateral Spontaneous Pneumothorax

There were 11 alternating and two simultaneous cases. None was of the progressive tension variety, and in only one was there severe dyspnea on admission. The term "alternating pneumothorax" is used in this series only where the contralateral lung had collapsed at least two months after the original side was completely expanded.

In eight of the 11 alternating pneumothoraces, thoracotomy was done on the side of the last attack. Blebs were found in all cases operated. These were removed, followed by pondrage and catheter decompression. There was only one recurrence, and this occurred three months later on the contralateral side. In one case the pneumothorax was treated by aspiration, one by glucose instillation and catheter decompression following thoracoscopy, and one by bed rest alone. There was no recurrence in these three cases. The one treated by bed rest required three months for expansion (refused treatment), and the one treated by thoracentesis took three and one-half weeks, whereas the eight operated were expanded at

the completion of operation and remained so, and the one treated by catheter decompression was expanded in a few minutes on one side, and on readmission four months later was expanded on the contralateral side in one day.

In the instance of the two simultaneous pneumothoraces, one was treated by bilateral simultaneous catheter decompression, one lung expanding in a few minutes and the other in two days. In the second case, immediate bilateral expansion occurred following catheter decompression and bilateral thoracotomy at four month intervals was done. Blebs were found on both sides. These were removed, poudrage done, and catheter drainage established.

Spontaneous Hemopneumothorax

The onset in four of the six cases was sudden, and all four were in varying degrees of shock when first seen. In the six cases, treatment consisted of multiple thoracenteses, and amounts of blood of 400 to 4,100 cc. were removed by thoracenteses over a period averaging five days. One of us (C.G.) suggested the use of hematocrit in testing samples of blood withdrawn at each thoracentesis in order to determine whether bleeding was continuing, of intermittent character, or had cleared. This ingenious idea has been used and found eminently satisfactory. It is also, we might add, of considerable value in attempting to make the diagnosis of continuing intrathoracic bleeding in trauma to the chest. No operative interference or catheter decompression was used in five cases. All were expanded by the end of two weeks. In the sixth case, expansion of the lung was impeded by a fibroplastic residual and this was decorticated. In two of the cases spontaneous hemopneumothorax occurred in alternating spontaneous pneumothoraces. In one case the hemopneumothorax occurred on the right, and later left spontaneous pneumothorax occurred. In the second case spontaneous pneumothorax occurred on the right, and later hemopneumothorax on the left.

Summary of Treatment of All Cases

Bed rest only	11
Thoracentesis only	18
Intercostal catheter decompression	17
Thoracoscopy with catheter decompression	12
Thoracoscopy with instillation of glucose and catheter decompression	11
Thoracoscopy with insufflation of talc and catheter decompression	5
Thoracotomy with removal of blebs and bullae, poudrage, and catheter decompression	28
Decortication	8
Phrenic emphraxis	1
Refused treatment	3
TOTAL PATIENTS	114

Discussion

Incidence. The incidence of unilateral spontaneous pneumothorax is far more than detailed in the literature. There must be numerous cases never

diagnosed, as the symptoms may be mild or absent and the case is therefore missed unless a roentgenogram is taken. Ten per cent of our cases had no symptoms, being found on routine chest films. In situations where roentgenograms are taken routinely or for even mild symptoms (Armed Forces hospitals), the number found is considerably more than in civilian practice. In the U. S. Army[20] 873 cases were reported as hospitalized in 1943. In 15 per cent it was found necessary to separate them from the Service because they were deemed sufficiently disabled.

Side involved. In our series the cases were equally divided as to right and left sides. Charr[21] reports more on the left side and credits this to more pulmonary motion due to cardiac action. This explanation is difficult to accept, as physical activity with obvious increase in ventilatory function seems not to be a factor. Leach[22] reports 38.8 per cent as having no physical activity, and mild or unstated activity in 50.4 per cent of 129 cases. In our series 20 per cent occurred in bed while resting alone, and in 30 per cent more there was only mild physical activity.

Recurrence rate. There were 47 cases of recurring spontaneous pneumothorax in our series, and when one adds the 11 bilateral and the 11 recurrences after treatment or refusal of treatment, the total is 69 recurrences out of 114 cases (60.5 per cent). The recurrence rate as reported is from 5 to 45 per cent.[4,23-27]

Etiology. There are many[4,7-10,12,13,28-39] excellent dissertations on etiology. Only a brief review of the experimental work and clinical substantiation is in order here, for it forms the basis of our ideas concerning, first, the active treatment of the first attack, and second, surgical intervention in recurrent cases. Kjaergaard[4] felt that spontaneous pneumothoraces were due to the rupture of subpleural vesicles of two types—one, a vesicle developing in the apex adjacent to old tuberculosis, and second, emphysematous vesicles occurring on the basis of localized emphysema without scar tissue. As the majority of vesicles and blebs are found in the apices, the observation of Ornstein and Lercher[26] concerning disproportionate overventilation of lung apices during a Valsalva maneuver may well explain the anatomical location. Macklin[7,8] pointed out on both experimental and clinical evidence that first there was atelectasis or some form of partial bronchial obstruction giving local obstructive emphysema with resultant break in the alveoli, permitting air to enter the pulmonary paravascular tissue. From the interstitial emphysema air traveled up and into the mediastinum. The mediastinal emphysema could then break into one or both pleural cavities and/or go up into the neck or even travel retroperitoneally. He also produced pneumothorax from experimentally produced mediastinal emphysema. One of us (L.M.S.) has seen cases of large bleb formation in certain pneumonias of childhood, and spontaneous pneumothorax in cases of severe dyspnea in bronchial foreign bodies and in "bull-neck" diptheria, all of these being evidences and results of obstructive emphysema. Hamman[9] furthered this contention in pointing out the clinical relationship between mediastinal emphysema and spontaneous pneumothorax. These contentions of Kjaergaard, Macklin, and Hamman

have many supporting clinical reports.[28-30,31-36,40] Hamman[9] reported that two cases out of 27 spontaneous pneumothoraces had mediastinal emphysema. Dickie[33] reported that in 20 patients, six had pneumothorax alone, seven pneumo-mediastinum, and seven had both.

Draper[28] points out that although spontaneous mediastinal emphysema and spontaneous pneumothorax may occur together, the vast majority of pneumothoraces occur without *demonstrable* mediastinal emphysema. We concur in this, for in our 114 cases, we did not see mediastinal emphysema in any, and in only one case could Hamman's sign[9] be heard. This patient was a physician in whom the crackling noise synchronous with the heartbeat was audible without a stethoscope; yet the mediastinal emphysema was not detected by roentgenograms. Wise[36] makes, we feel, an important point in stating that in many cases of spontaneous pneumothorax in which mediastinal emphysema was not recognized previously, the symptoms are severe and similar to those with spontaneous pneumothorax. Perhaps when cases require differential diagnosis between coronary occlusion, dissecting aneurysm, ruptured peptic ulcer (Hamman[9] and Miller[34]), and spontaneous pneumothorax, and if no air is seen in the pleural cavity, the precordium should be *carefully* and *repeatedly* auscultated and a search for roentgenographic evidence of mediastinal emphysema should be done *repeatedly*.

The facts and theories as substantiated by clinical and experimental evidence are not, as at first glance, contradictory, for whether there is an escape of air directly from the "valvevesicle" (Kjaergaard) into the pleural cavity, or from the mediastinum (Macklin), both require certain changes in the lung parenchyma (localized obstructive pulmonary emphysema—Macklin, or localized emphysema on the basis of scar tissue—Kjaergaard). It may be presumptuous to interpret other men's experimental work, but on the basis of our clinical experience it might not be unreasonable to assume that these two are different phases of the same or similar processes, Macklin's being more of the acute type, whereas Kjaergaard's statements as to pathogenesis obviously refer to lesions that require time to evolve. Perhaps the vesicle or bleb may result quickly, but the "scar" of the lung parenchyma requires time.

Methods and Basis of Treatment

In general, we feel that whether the source of air leaking into the pleural cavity is directly from the vesicle or bleb, or indirectly from such sources via the mediastinum, the problem is one of overcoming the effects on the lungs. If the leak is directly from the vesicle or bleb, it is obvious from the results that sudden expansion of the immediate adjacent normal, but collapsed, lung stops the leak. If we consider the indirect route (interstitial emphysema and mediastinal emphysema) being treated by immediate expansion, we have an even better basis for such treatment. This route requires the presence of partial atelectasis of at least a segmental or sub-segmental degree. Under such circumstances, leaking of air into the pulmonary parenchyma from the emphysematous area distal to the partial atelectasis would certainly continue or tend to be prolonged, as the factor

of air drift could not be effective. There could be no air drift across a segmental plane if the segments adjacent to the one containing the partial atelectasis are collapsed as part of the pneumothorax.

It is often difficult to visualize bullae by roentgenogram and only rarely can one see vesicles or blebs. Sycamore[41] demonstrated the fact that bullae can be seen after reexpansion of the lung. Kjaergaard,[4] Gordon,[42] and Castex and Mazzei[43] have discussed this problem. The difficulty of visualizing any abnormality by roentgenogram with exception of the pneumothorax is commonly encountered. Bullae and blebs have in our experience been most evident when the lung was collapsed or in the process of expansion. The absence of such findings on roentgenogram does not constitute contraindication for surgery, for in the combination of our series and those of Brock,[15] Meade and Blades,[16] Brewer, Dolley and Evans,[12] and Haver and Clagett,[17] 91 per cent had blebs, bullae, cysts, etc., found at operation.

Spontaneous pneumothorax — Initial attack. Considering the relative greater speed and expansion of the greater percentage of such cases by intercostal catheter decompression, as compared to bed rest alone or bed rest and intermittent thoracenteses, we can find no reason for not interfering where possible as promptly as possible. The expansion of the greatest majority of cases in from a few minutes to two days, as compared to an average of three weeks, is important from an economic standpoint. In these days of not only a shortage of hospital beds, but also high cost of hospitalization and economic loss to the patient hospitalized for long periods, this time differential should be of great significance.

The natural reluctance to put a foreign body (i.e., catheter) into the pleural cavity in a type of case in which the majority will *eventually* resolve themselves is understandable, but we would like to point out that in the 37 cases in which intercostal catheters were installed by 11 different operators, there were no complications (no infections and no residual complications). Considering the absence of complications, the ease and rapidity of treatment, and the relative lessened economic cost, we feel this is by far the choice of treatment. In addition to these factors, the obvious advantage of immediately reducing or eliminating pleural complications of infection and/or unexpanding lung is of value even in the few cases in which these complications occur following the initial attack.

The routine of our use of intercostal catheter decompression is approximately as follows: As soon as there is roentgenographic evidence of spontaneous pneumothorax, an intercostal catheter varying from 16 to 20 French is inserted via trocar under local anesthesia in the second interspace anteriorly in the male, and in the anterior axillary line high in the axilla in the female just posterior to the lateral edge of the pectoralis major muscle. This is immediately attached to a water trap and the patient is asked to cough repeatedly or strain after deep inspiration with closed glottis, following which a portable semi-sitting or erect roentgenogram is made. If the lung is found to be completely expanded, the roentgenogram is repeated in 12 hours, and if the lung is still expanded at that time, the catheter is left in place but clamped. The roentgenogram is then repeated 12 hours

later, and if the lung is fully expanded, the catheter is removed. In the removal one should be careful not to permit any air to escape into the pleural cavity. A safe way to do this is to have the patient hold a deep breath and strain against the closed glottis during the removal. This technique is used whether the intercostal catheter decompression is used alone or in conjunction with instillation of glucose or insufflation of talc.

In the majority of cases treated by catheter and water trap decompression, the lungs were expanded without suction. In four after elapse of 24 hours without adequate expansion—constant suction of 10 to 14 cm. of water was used. This is a helpful adjunct to the therapy.

The use of a needle placed in the pleural cavity and fixed to the chest wall (Chandler,[44] Marriott and Foster-Carter[45]) appears to us to have the disadvantage of being easily dislodged and readily blocked. We feel that if one wishes to permit a *constant* egress of air from the pleural cavity, a catheter and not a needle should be used.

The advantage of earlier expansion by catheter decompression is shown by Hughes and Lowry[46] who averaged 11½ days for expansion in 27 out of 40 cases in which a catheter was used. As comparison they point out average expansion times without catheters as follows:

1 to 4 weeks - - - - -	Ornstein and Lercher[26]
4 weeks - - - - - - -	Rottenberg and Golden[47]
7 weeks - - - - - - -	Hyde and Hyde[48]
1 to 9 weeks - - - - -	Niehaus[49]
6 weeks to 2½ months -	Kjaergaard[4]

Recurrent attacks and chronic pneumothorax. Following our reasoning as the basis for treatment in our initial attacks, and considering the percentage of recurrences, it is logical then to either decompress immediately by catheter and/or follow up by thoracotomy in recurrent and chronic pneumothoraces. Those in distress due to the degree of loss of functioning pulmonary parenchyma are first decompressed and expanded by catheter, or at least decompressed by catheter, and then when the patient is without dyspnea, we follow this by thoracotomy. Patients not dyspneic are not decompressed if a thoracotomy is to be done. In those advanced in age or with associated marked pulmonary emphysema, or heart disease, or a combination of all three, treatment may end with expansion of the lung by catheter. This conservatism is open to some question, for a patient with lowered pulmonary function and/or cardiac reserve is more distressed and is certainly less capable of surviving repeated attacks of sudden reduction in pulmonary function than one who is otherwise well. We have taken this into account, and in 24 of the 34 recurrent cases of spontaneous pneumothorax operated, two had reduced cardiac reserve, one had considerable pulmonary emphysema and arteriosclerotic heart disease, and one was 73 years of age, besides being emphysematous with beginning cor pulmonale. Age in itself does not constitute a contra-indication for operation.

Thoracotomy in these cases consists of posterolateral incision, opening of the pleural cavity by rib resection or intercostal approach, removal of

blebs, bullae, or cysts by clamping relatively good lung proximal to the base of the lesion, and excision and suture closure (a second layer enfolds the first suture line). Airtight closure is checked by filling the pleural cavity with saline and having the anesthetist expand the lung with positive pressure. The saline is then removed and talc is placed on the costal surfaces of the lobes. Care is taken to keep the talc out of the mediastinum, off the mediastinal surface of the lobes, and off the diaphragmatic surface of the lower lobes. As the talc is placed, care is also taken to see that the chest wall muscle layers are not dusted by it. Intercostal drainage, antero- and posterolateral, is established and attached to water traps, and closure of the thoracotomy is done while the lung is inflated.

Operative interference in the past, as shown by reports, has a firm basis in the operative findings. Brock[15] (1948) operated eight of 46 cases, finding large cysts requiring excision or resection by lobectomy. Meade and Blades[16] (1949) reported eight recurrent and 11 chronic cases operated. In the eight recurrent cases, five had multiple blebs, and only in three were no findings noted. In the 11 chronic cases, three had ruptured bronchogenic cysts, five had leaking blebs, one had a bronchopleural fistula held open by an adhesion, and in only two were no causes found. Brewer, Dolley and Evans[12] (1950) found ruptured congenital cysts, blebs, or bullae in 14 out of 15 cases. Thus, in a total of 41 cases operated[12,15,16] there were obvious pathological findings in 35. In our series of 37 thoracotomies on 36 patients (one bilateral thoracotomy), findings of blebs, bullae, or cysts were noted in 33.

Cases which fail to respond promptly to methods of expansion have been shown by numerous authors to become chronic pneumothoraces in a considerable percentage. Haver and Clagett,[17] Babington,[50] Elghammer,[51] Hedgpeth et al,[52] Ehrlich,[53] and Kjaergaard[4] have all shown that if the pneumothorax is left unexpanded long enough, it will fail to expand. Thus, by temporizing and waiting in the case of chronic pneumothorax, one may have to decorticate the lung, as well as remedy the source of the leak, when surgery is finally done.

Bilateral spontaneous pneumothorax. The incidence as reported in the literature is, we feel, as with the unilateral spontaneous pneumothorax, no true index of its frequency. The understandable reluctance to report a single case, or at the most a few cases, certainly contributes to this. Oechsli[54] reviewed the literature up to 1934 and reported 77 bilateral spontaneous pneumothoraces. Glickmann and Schlomovitz[55] in 1936 increased this by review of the literature to 82 cases. Cooch[30] by 1948 collected 44 alternating spontaneous pneumothoraces to which he added one. Our addition of 13 cases (alternating and simultaneous pneumothoraces) is an indication that approximately 10 to 12 per cent of any large series of spontaneous pneumothoraces will be of the bilateral variety.

In instances of alternating collapse of the right and left lungs, unless there is a strong contra-indication to surgery, the patient should be given the protection of at least one lung that will remain expanded. This protection is even more important in cases of simultaneous collapse. There is no question in our minds that it is not elective, but imperative, that at

least one side be operated. Actually the same treatment should be afforded both types of cases, for it is purely fortuitous whether the patient is seen at any given time with an alternating or a simultaneous collapse. Three of our alternating pneumothorax cases gave a history of previous simultaneous collapse (one having had simultaneous collapse twice), and one of the two simultaneous cases gave a history of four attacks of previous alternating collapse.

Spontaneous hemopneumothorax. Kjaergaard[4] reported two out of 51 spontaneous hemopneumothoraces in the literature up to 1932. After a period of 10 years (1942), Hartzell[56] found 40 in the literature and added three of his own. In 1952 Holloway, Speir and Sadler[14] found 80 reported cases up to 1950 with 20 per cent mortality. All agree that the source of the bleeding is the tearing of a vascular adhesion with bleeding from either end of the adhesion. Holloway et al,[14] in their excellent article present cases demonstrating the need for thoracotomy. Their indication is soundly based, as is any indication for thoracotomy, in continued intrathoracic bleeding.

As stated, none of our six cases was operated because of continued bleeding. In reviewing the cases in detail, we feel that two of them were extremely fortunate to have survived with the only treatment being that of multiple thoracenteses. If the bleeding is from the pulmonary side of the torn adhesion, immediate expansion of the lung might be curative, depending on whether the bleeding is from the pulmonary or systemic circuit. Furthermore, it is most doubtful if pulmonary expansion will stop bleeding from the chest wall side unless it is part of a huge clot. Such a circumstance would hardly be desirable, for then the patient would surely require far more surgery (decortication).

In the future, we will follow the lead of Holloway et al,[14] in cases of continued bleeding and operate to ligate the source. With our knowledge today of blood replacement, it is not unreasonable to assume that the patient can be brought to surgery in relatively good condition and at a time most suitable for his survival.

SUMMARY

We feel that all initial spontaneous pneumothoraces, unless practically expanded when first seen, should be promptly treated by intercostal catheter decompression. All cases of recurrent spontaneous pneumothorax, chronic pneumothorax, and bilateral recurrent pneumothorax should be treated by surgery as described. Spontaneous hemopneumothorax should be treated by prompt and energetic thoracentesis and operated when there is evidence of continuing intrapleural bleeding.

RESUMEN

Creemos que todo neumotórax espontáneo inicial que no sea expandido cuando se ve por primera vez, debe tratarse inmediatamente por descompresión por la vía intercostal por medio del catéter. Todos los casos de neumotórax espontáneo recurrente y de neumotórax espontáneo bilateral

y neumotórax espontáneo crónico, deben tratarse por la cirugía como se ha descrito. El hemoneumotórax espontáneo, debe tratarse prontamente por toracentesis y se debe operar cuando hay evidencia de hemorragia intrapleural continua.

RESUME

Les auteurs estiment que les pneumothorax spontanés apparaissant pour la première fois devraient être rapidement traités par exsufflation à l'aide d'une ponction intercostale, sauf dans les cas où il sont pratiquement déjà en réexpansion quand ils sont vus. Tous les cas de pneumothorax récidivants bilatéraux devraient être traités chirurgicalement ainsi que les auteurs le décrivent. L'hémo-pneumothorax spontané doit être traité par une rapide et importante thoracenthèse et opéré quand il y à des signes d'hémorragie intrapleurale persistante.

REFERENCES

1 Itard, J. E. M. G.: "Sur Le Pneumothorax, Ou Les Congestions Gazeuses Qui Se Forment Dans La Poitrine," *Paris Ann.*, 11, 1803.
2 Laennec, R. T. H.: "Traite-de L'Auscultation Mediate et des Maladies des Poumons et du Coeur," 2 Ed., 2 V., 36:728, 4 pl.; 790 pp. 11.80 Paris; Claude 1826.
3 McDowell: "On an Unusual Form of Pneumothorax," *Dublin Hosp. Gaz. n.s.*, 3:227, 1856.
4 Kjaergaard, K. H.: "Spontaneous Pneumothorax in the Apparently Healthy," 252: Leven and Munksgaard, 1931, Copenhagen. "Spontaneous Pneumothorax in the Apparently Healthy," *Acta. Medica. Scand.*, 1:Supp. 43, 1932. "Pneumothorax Simplex," *Acta. Medica. Scand.*, 80:93, 1933.
5 Leggett, E. A., Myers, J. A. and Levine, I.: "Spontaneous Pneumothorax, Report of 31 Cases," *Am. Rev. Tuberc.*, 29:348, 1934.
6 Blackford, S. D.: "Spontaneous Pneumothorax in College Students," *J.A.M.A.*, 113:737, 1939.
7 Macklin, C. C.: "Pneumothorax with Massive Collapse from Experimental Local Over Inflation of Lung Substance," *Canad. M. A. J.*, 36:414, 1937.
8 Macklin, C. C.: "Transport of Air Along Sheaths of Pneumonic Blood Vessels from Alveoli to Mediastinum; Clinical Implications," *Arch. Int. Med.*, 64:913, 1939.
9 Hamman, L.: "Spontaneous Mediastinal Emphysema (Henry Sewall Lecture)," *Bull. Johns Hopkins Hosp.*, 64:1, 1939.
10 Emerson, C. P.: "History of Our Knowledge of Pneumothorax from Earliest Times to 1903," *Johns Hopkins Hosp. Reports*, 11:1, 1903.
11 Crenshaw, G. L.: "Etiology, Treatment, and Surgical Indications of Non-Tuberculous, Non-Traumatic Spontaneous Pneumothorax," *Dis. of Chest*, 17: 369, 1950.
12 Brewer, L. A., Dolley, F. S. and Evans, B. H.: "The Surgical Management of Chronic 'Spontaneous' Pneumothorax," *J. Thoracic Surg.*, 19:167, 1950.
13 Fischer, B.: "Der gutartige Spontanpneumothorax dur Ruptur von Spitzennarbenblasen ein Typisches Krankheitsbild," *Zeitsch. f. Klin. Medizin*, 95:1, 1922.
14 Holloway, J. B., Speir, R. C. and Sadler, R. N.: "Spontaneous Hemopneumothorax Requiring Thoracotomy," *Am. Surg.*, 18:518, 1952.
15 Brock, R. C.: "Recurrent and Chronic Spontaneous Pneumothorax," *Thorax*, 3:88, 1948.
16 Meade, R. H. Jr. and Blades, B. B.: "The Surgical Treatment of Recurrent and Chronic Spontaneous Pneumothorax of Non-Tuberculous Origin," *Am. Rev. Tuberc.*, 60:683, 1949.
17 Hover, Louis P. and Clagett, O.: "Treatment of Chronic Spontaneous Pneumothorax by Lobectomy," *J. Thoracic Surg.*, 15:418, 1946.
18 Curti, P. C. and Poulsen, T.: "Treatment of Simple Spontaneous Pneumothorax," *J. Thoracic Surg.*, 19:145, 1950.
19 Churchill, E. D.: Personal communication as quoted by Tyson, M. D. and Crandall, W. B.: "The Surgical Treatment of Recurrent Idiopathic Spontaneous Pneumothorax," *J. Thoracic Surg.*, 10:566, 1940.
20 *Bull. U. S. Med. Dept.*, 82:29, 1944.
21 Charr, Robt.: "Spontaneous Pneumothorax," *Am. Rev. Tuberc.*, 40, 1938.

22 Leach, J. E.: "Pneumothorax in Young Adult Males; Descriptive Data on 126 Cases," *Arch. Int. Med.*, 76:264, 1945.
23 Cohen, S. and Kinsman, J. M.: *New Eng. J. Med.*, 235:461, 1946.
24 Wilson, J.: *Internat. Clinics*, 1:151, 1939.
25 Schneider, L. and Reissman, J.: *Am. J. Roent.*, 54:12, 1947.
26 Ornstein, G. G. and Lercher, L.: *Quart. Bull. Sea View Hosp.*, 7:149, 1942.
27 Wood, H. G.: *Miss. Med.*, 14:550, 1931.
28 Draper, A. J.: "Spontaneous Mediastinal Emphysema and Pneumothorax," *Am. J. Med.*, 5:59, 1948.
29 Hyde, B. and Hyde, L.: "Spontaneous Mediastinal Emphysema and Bilateral Spontaneous Pneumothorax," *Am. Rev. Tuberc.*, 61:883, 1950.
30 Cooch, J. W.: "Alternating Idiopathic Spontaneous Pneumothorax," *Southern Med. Jr.*, 41:1094, 1948.
31 Adcock, J. D.: "Spontaneous Interstitial Emphysema of Lung; With Mediastinal, Retroperitoneal, and Subcutaneous Emphysema," *Arch. Int. Med.*, 71:650, 1943.
32 Lintz, R. M.: "Spontaneous Mediastinal Emphysema," *Arch. Int. Med.*, 71:256, 1943.
33 Dickie, H. A.: "Spontaneous Mediastinal Emphysema and Spontaneous Pneumothorax—Report of 20 Cases," *Ann. Int. Med.*, 28:618, 1948.
34 Miller, T.: "Spontaneous Interstitial Emphysema of Lung: Report of Two Cases and Summary of Literature," *Ohio State M. J.*, 37:1056, 1941.
35 Morey, T. B. and Sosman, M.: "Spontaneous Mediastinal Emphysema with Report of One Case Associated with Spontaneous Pneumothorax," *Radiology*, 32: 19, 1939.
36 Wise, R. A.: "Idiopathic Spontaneous Pneumothorax," *Texas State Jr. Med.*, 46:889, 1950.
37 Bernon, A. and Neumann, J.: "Etiology of Spontaneous Pneumothorax: Role of Rupture of Subpleural 'Bubbles,' Roentgenogram Study of Case," *Rev. de. La Tuberc.*, 1:1170, 1935.
38 Desmeules, R.: "Pneumothorax Spontane Avec Symptomotalogie Rare," *Am. Rev. Tuberc.*, 4:284, 1939.
39 Wilson, S. R.: "Bilateral Spontaneous Pneumothorax," *Lancet*, 2:136, 1934.
40 McKay, D. R.: *N. Y. State Jr. Med.*, 50:182, 1950.
41 Sycamore, L. K.: "Recurrent Idiopathic Spontaneous Pneumothorax," *Am. J. Roentg.*, 36:844, 1936.
42 Gordon, J.: "Benign Spontaneous Pneumothorax," *Lancet*, 2:178, 1936.
43 Castex, M. R. and Mazzei, S.: As quoted by Tyson and Crandall.[19]
44 Chandler, F. G.: "Valvular Pneumothorax Treated by Mechanical Valve and Obliterative Pleurisy," *Lancet*, 2:638, 1939.
45 Marriott, H. L. and Foster-Carter, A. F.: "A Simple Apparatus for Constant Suction," *Lancet*, 1:122, 1940.
46 Hughes, F. A. and Lowry, C. C.: "Treatment of Idiopathic Spontaneous Pneumothorax," *J.A.M.A.*, 46:244, 1951.
47 Rottenberg, L. A. and Golden, R.: "Spontaneous Pneumothorax; Survey of 105 Cases," *Radiology*, 53:157, 1949.
48 Hyde, B. and Hyde, L.: "Benign Idiopathic Spontaneous Pneumothorax; Review of 63 Cases," *Am. J. Med. Sci.*, 215:427, 1948.
49 Niehaus, R. F.: "Simple Spontaneous Pneumothorax in Apparently Healthy Individuals; Report of 24 Cases," *Am. J. Roentg.*, 57:12, 1947.
50 Babington, S. H.: "Idiopathic Spontaneous Pneumothorax," *West. J. Surg.*, 52: 73, 1944.
51 Elghammer, H. W.: "Spontaneous Tension Pneumothorax; Report of Case," *Arch. Pediat.*, 53:490, 1936.
52 Hedgpeth, E. McG., Berryhill, W. R., Morgan, W. G., Stone, R. E., Patterson, F. G. and Smith, R. A.: "Spontaneous Pneumothorax; Diagnosis and Prognosis," *N. Carolina M. J.*, 5:48, 1944.
53 Ehrlich, D. E. and Schomer, Alexander: "Spontaneous Pneumothorax," *Radiology*, 30:471, 1938.
54 Oechsli, W. R. and Miles, S. H.: "Simple Bilateral Spontaneous Pneumothorax," *Am. Rev. Tuberc.*, 30:239, 1934.
55 Glickman, L. G. and Schlomovitz, B. H.: "Simple Bilateral Spontaneous Pneumothorax Complicating Pneumonoconiosis," *Am. Rev. Tuberc.*, 34:390, 1936.
56 Hartzell, H. C.: "Spontaneous Hemopneumothorax," *Ann. Int. Med.*, 17:490, 1942.

Bronchogenic Carcinoma in East Pakistan

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Introduction

At the turn of this century primary carcinoma of the lung was considered a rare disease but it has shown an amazing upsurge during the last 50 years. In some of the western countries more particularly the United States of America and the United Kingdom it now claims a higher toll of human life than gastric carcinoma which previously topped the list of death ascribed to cancer.

Three factors have been invoked to explain this alarming increase in the incidence of this disease. First, it is averred that the increase in the primary bronchogenic carcinoma may not be actual but may be due to its more frequent detection than formerly because of improvements in clinical diagnostic methods and pathological technique.

Second, it is ascribed to the change in the pattern of life brought about by the industrial revolution, especially the large scale mechanisation of transport and the universal use of automobiles, particularly in countries such as the United States of America.

Third, it is held that heavy smoking as reflected in the increase in production and sale of cigarettes during the last 50 years may be a causative factor. Investigations have sought to establish a direct relationship between the increase in bronchogenic carcinoma and cigarette smoking.

Thus, in the United States of America a great majority of the proved cases of bronchogenic carcinoma were found to have been amongst those addicted to heavy smoking for years. A corroborative observation is that, taken by and large, the bronchogenic carcinoma of the lung, especially the epidermoid type, is a disease of the male. In the event of a woman being the victim she has usually been observed to have been a heavy smoker.

The object of this paper is to record my experiences of this disease as observed in the Dacca Medical College Hospital which is about the only well-equipped hospital in East Pakistan with a population of 43 million people. The country is mostly under-developed and 90 per cent of its people live in villages leading an open air and agrarian life. Use of automobiles and the existence of tarred roads touch a microscopic fringe of the general population. The system of road communication is extremely undeveloped, the usual mode of transport being the country boats and bullock carts.

Materials:

My observations on primary carcinoma of the lung began towards the end of 1950 when I took charge of 40 beds (30 males and 10 females) in the Dacca Medical College Hospital. The admission of patients followed

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the normal procedure, the only criterion of admission being the relative urgency of the condition of the patient. As a consequence, cases of remittent fever, pneumonias, appoplexy, nephritis and heart disease preponderated. Over a period of 18 months, total admissions to my ward were 1,586 of which 362 were cases of pulmonary disease, comprising chiefly the commoner affections such as lobar pneumonia, bronchial asthma, bronchiectasis, lung abscess, primary pleural effusions, etc. Amongst these, however, 20 cases were detected to be suffering from bronchogenic carcinoma. Unfortunately data of this disease in the hospital records during preceding years is not supported by requisite clinical and pathological investigations to be of statistical value.

Diagnosis:

The following points were stressed in clinical examination and investigation:

I) Clinical History: Any patient aged 40 or above, with a history of haemoptysis for the first time was presumed to be a case of bronchial carcinoma unless it was proved otherwise.

II) Sudden appearance of respiratory complaints such as cough, breathlessness, localized pain in the chest in the above age-period were considered suspicious and were thoroughly investigated.

III) Neurological conditions as hemiplegia with Jacksonian convulsion in the paralyzed limb or with bilateral extensor planter reflex indicated special chest examination to exclude bronchogenic carcinoma.

Investigation:

The following investigations were done as a routine:

(i) Blood counts and sedimentation rate; (ii) sputum examination for acid-fast bacilli, fungi and malignant cells; (iii) Fluoroscopy and radiography of the chest both postero-anterior and lateral. When indicated, the following examinations were also carried out:

(i) Bronchography; (ii) bronchoscopy; (iii) biopsy of the axillary or cervical lymph nodes whenever enlarged; and (iv) surgical exploration (one case only).

Facilities:

In the absence of a chest unit no proper facilities yet exist for thoractomy or pneumonectomy, but a few Pakistani doctors are receiving special training in this branch of surgery. Autopsy was performed on two cases only, as permission to carry out post-mortem is extremely difficult to secure for religious and sentimental reasons. Consequently, reliance had to be placed on clinical investigations and sputum examination for malignant cells.

Analysis of Cases:

Detailed protocols of the cases in this series are given in Appendix. The salient features are tabulated below:

TOTAL NUMBER OF CASES, 20.

Sex:

Male	18
Female	2
TOTAL	20

Age (in years):

40-49	9
50-59	4
60-70	6
71-80	1
TOTAL	20

OCCUPATION:

Male	Cultivator (Paddy and Jute field laborers)	11
	Land Lord	2
	Business man	2
	Police Constable	1
	Clerk (Village school)	1
	Health Assistant	1
Female	Housewives	2
	TOTAL	20

ENVIRONMENT:

Villagers (who never visited town before admission):

Male	11.
Female	1

Born and brought up in town:

Male	1
Female	1

Villagers (who visited town occasionally:

Male	6
TOTAL	20

SMOKING HABITS:

Heavy smokers:

Male	2

Occasional smokers:

Male	4

Non-smokers:

Male	12
Female	2
TOTAL	20

Method of smoking is somewhat different in this country in that the great majority of the people rarely smoke cigarettes. They use a locally made pipe known as "Hukka" in which the smoke passes through water before being inhaled. Crude tobacco is also smoked rolled up inside a "biri" leaf.

SYMPTOMS AND SIGNS IN ORDER OF FREQUENCY:

Symptom	Number of Cases in Which Present	Duration
Cough	17	6 months to 2 years
Dyspnoea	15	6 months to 2 years
Pain in chest	10	3 to 6 months
Haemoptysis	10	4 to 10 months
Clubbing of fingers	8	Noticed during examination
Dysphagia	2	1 to 2 months
Enlarged nodes	2	1 to 3 months
Hoarseness of voice	1	2 weeks
Hemiplegia with,		
Jacksonian convulsion	1	1 month
with aphasia	1	3 months
Horner's syndrome	1	2 weeks
Fever, simulating pneumonia, pneumonitis with one or more of the above symptoms	8	3 to 6 months
PREVIOUS ILLNESSES:		
Malaria	9	
Pneumonia	3	
Pulmonary tuberculosis	1	
Recurrent coryza in winter	3	
Dysenteric symptoms	6	
Heminthiasis:		
Round worm	5	
Hook worm	3	

Case 1: W.M., a muslim male, landholder, of 40 years, admitted on December 26, 1950 with cough, profuse expectoration, dyspnoea especially on lying down, progressive loss of weight and pain on the right side of his chest for nine months. Occasional fever, insomnia and anorexia supervened in the last two months.

Past illness of recurrent attacks of malaria for eight years.

He was a non-smoker.

Clinical examination: Well built but emaciated, markedly anaemic and dyspnoeic. There was moderate clubbing of fingers. T—990F, P/R=120/40 per min., B/p—106/72. Chest: Mediastinum Central. Sign of Consolidation on the right side. No abnormality in any other system. Blood: haemoglobin, 40 per cent; red cell, 2.5 million per cmm.; white cell count, 16,000 per cmm. with 80 per cent neutrophils; sedimentation rate, 65 mm./hr. Sputum, no acid-fast bacilli or fungi. Malignant cells present, epidermoid type. X-ray film revealed haziness on the right midzone with enlarged hilum shadow. There was a suspicion of erosion of fourth and fifth ribs. A penetrating film showed the erosion more clearly.

Remarks: General condition improved with antibiotics and supportive treatment but he left the hospital on January 31, 1951 on risk bond. At home he developed an abscess on the right side of inter-scapular region and he expired on February 2, 1952.

Case 2: M.H., a Muslim male, non-smoker, cultivator of 42 years was admitted on March 7, 1951 with the history of cough with blood-stained sputum, pain in the right side of the chest, irregular fever, progressive loss of weight for five months. Past history of malaria, dysentery and round worm for six years back.

Clinical examination: Build and nutrition fair, anaemic with early clubbing of fingers.

Chest examination: Revealed impaired resonance and diminished breath sounds with few moist sounds at the middle zone posteriorly. Other systems were found normal except a firm and three finger enlarged spleen.

Investigation: Blood picture was found normal except slight anaemia. Sedimentation rate, 70 mm./hr. Sputum examination showed malignant cells but no acid-fast bacilli or fungi. X-ray film revealed collapse of right middle lobe; bronchoscopy showed narrowing of the right middle lobe bronchus.

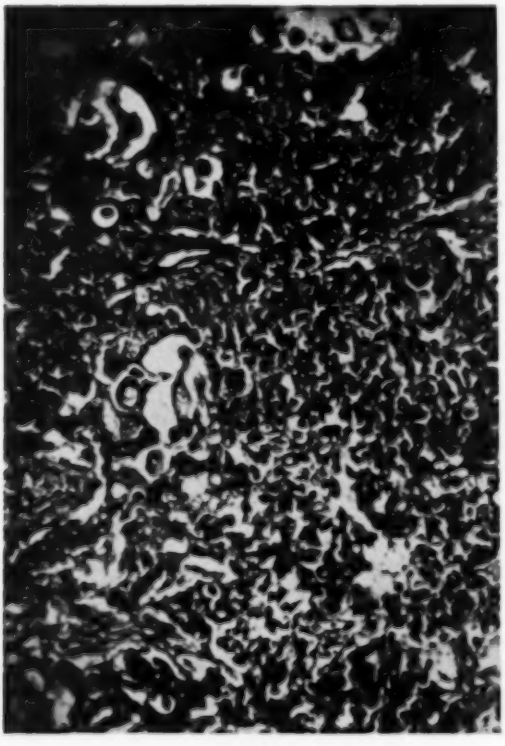
Progress: Haemoptysis and fever controlled, weight gained by four pounds after antibiotic and supportive treatment and was discharged.

Case 3: Z.A., a non-smoking Muslim male cultivator of 40 years was admitted on April 17, 1951 with a two month history of cough with expectoration, haemoptysis in moderate quantity and gradual loss of weight. Past history of cholera two years and malaria eight years back, pneumonia during childhood.

Clinical examination: Fair build and nutrition with clubbed fingers and anemia. T—99F, P/R—100/24 per min. Chest signs of collapse of the lower zone of the right lung. Other system normal.

Investigations: Blood picture was normal. Sedimentation rate, 50 mm./hr. Sputum examination revealed malignant cells but no acid-fast bacilli or fungi. X-ray film showed collapse of the right lower lobe. Bronchography revealed obstruction in the right lower lobe bronchus. Thoracotomy was done and he expired within a few hours. Autopsy showed bronchogenic carcinoma right lower lobe bronchus.

Case 4: Mrs. M.H., a Muslim married lady of 50 years was admitted on July 11, 1951 with a six month history of pain and swelling over the sternum, cough with scanty expectoration; and a recent history of swelling of left side of the neck with



CASE 3

tingling and burning sensation over the lateral half of her left hand, especially over the dorsum of left thumb, index and lateral half of middle finger. Past history of dysentery, 2 years back. Personal history, she was born and brought up in town, never smoked.

Clinical examination: Build and nutrition fair, moderately anaemic. Glands enlarged, hard and matted and very painful over the left supraclavicular and axillary region. T—99F. P/R—110/26 per min. Chest finding: a localized tender swelling about two inches in diameter was present over the manubrium. Diminished movement, impaired resonance and diminished breath over the left infra axillary region. Other system normal excepting diminished sensation over the distribution of the radial nerve.

Investigations: Blood picture moderate leucocytosis. Sedimentation rate, 55 mm./hr. Sputum, no acid-fast bacilli or malignant cells. X-ray film, an oval opacity in the left mid-zone bordering the chest wall. Biopsy of a cervical lymph node revealed adeno-carcinoma.

Remarks: Patient expired after 10 weeks at her residence.

Case 6: A.R., a Muslim male cultivator aged 50 years was admitted on October 14, 1951 with complaints of exertional dyspnoea and progressive loss of weight for one year, pain left side of the chest and dry cough for four months. He was a non-smoker. Had recurrent attacks of malaria for eight years and ankle lostomiasis for six years.

Clinical examination: He was fairly well built but very poorly nourished, markedly anaemic, and dyspnoeic. Odema present over the ankles and legs. Axillary and left supraclavicular lymph nodes palpable. P/R—104/38 per min. T—99F. B.P.—102/62 mm. of Hg. Chest findings, shifting of the mediastinum towards the right side. Cardiac apex was at fourth right intercostal space on the midclavicular line. Lung findings, signs of pleural effusion on the left side. No other abnormality.

Investigations: Haemoglobin 58 per cent, sedimentation rate 112 mm./hr. Sputum, no acid-fast bacilli or fungi seen. Malignant cells present. Pleural fluid was haemorrhagic. Biopsy of a right axillary lymph node showed metastatic malignancy. X-ray film revealed massive effusion on the left side.

Remarks: He signed the risk bond after three weeks stay in the hospital. His condition deteriorated.

Case 10: A.U. was a Muslim male aged 50 years, a village business man who was admitted on February 13, 1952 with a one month history of loss of power of right

CASE 10

extremities which started suddenly in the hand gradually involved his right arm, right thigh and leg.

Past history: Had attacks of dysentery and round worm infection for 20 years. Never smoked tobacco and visited town only twice after 1947.

Clinical examination: No anaemia, cyanosis or clubbing of fingers. Nervous system revealed upper motor neurone type of lesion of the right side. No sensory or visceral disturbance. Chest revealed no abnormality except a few crepitations in both bases. Other system normal. B/P—110/70.

On the night of admission at about 11 p. m. he suddenly started having spasms over his paralyzed arm which subsequently spread over the entire right side of the body. He did not lose consciousness and the attack continued for about 20 minutes. Next morning it was suspected to be a case of cortical lesion and he was screened in search of a primary focus. A rounded opacity was seen over the upper zone of the right lung.

His blood picture showed no significant change. Wasserman's Reaction, negative. Sputum, not available as he had no cough. X-ray film revealed a rounded circumscribed shadow in the right upper lobe.

He deteriorated rapidly with repeated convulsions and became unconscious before his death after a week. A partial post-mortem was done which revealed bronchogenic carcinoma in the posterior segmental bronchus of the right upper lobe. A growth occupying the upper half of the precentral gyrus was found on his left cerebrum.

Conclusions

Although the period of study of this disease has been short, certain interesting features emerge from the analysis of the data presented. It will be observed that bronchogenic carcinoma is prevalent in East Pakistan to a significant degree even amongst those who are not in contact with tarred roads, who lead mostly an open air rural life and who are not addicted to cigarette smoking. A high proportion of cases gave a long antecedent history of cough and dyspnoea, but these symptoms are so common in persons of advanced age-groups that the patients disregarded them and rarely sought medical advice until collateral distressing symptoms supervened, such as, haemoptysis, pain in the chest, hoarseness of voice and dysphagia. In other cases the presenting syndrome were totally non-pulmonary in character such as hemiplegia, aphasia or a lump in the axilla or neck.

Cancer consciousness on the part of the physician was the most important factor in the diagnosis of these cases. Clinical examination in most of these cases revealed restriction of movement of one side of the chest or shifting of the mediastinum associated with clubbing of fingers, enlarged glands, etc.

This series confirms the preponderance of the disease amongst the males, the proportion of male to female patients being nine to one.

Occupational factors did not appear to influence the occurrence of the disease. Although bronchogenic carcinoma is known to give rise to widespread blood borne metastases, only cerebral and lymph node (cervical and axillary) metastases were detected in these cases.

SUMMARY

1) Clinical data obtained from 20 cases of bronchogenic carcinoma observed during 18 months in Dacca Medical College Hospital, East Pakistan, have been analyzed.

2) Eighteen of these cases hailed from rural areas, where few tarred roads and automobiles are to be found. In most of the cases heavy smoking was not a factor.

3) Cough, dyspnoea, pain in the chest or haemoptysis in a person aged 40 years or above, should arouse suspicion of bronchogenic carcinoma and entail prompt and thorough investigation.

4) Cancer-consciousness on the part of the physician was found to be the determining factor in the diagnosis of these cases.

5) The series serves to bring out the fact that bronchogenic carcinoma is prevalent in East Pakistan to a significant degree. In the absence of reliable previous data its trend could not be determined. Further study of the disease is, therefore, of the utmost importance particularly with reference to etiologic or contributory factors other than tar or cigarette smoking.

Acknowledgment: I am indebted to Col. M. K. Afridi, Surgeon General with the Government of East Pakistan, for his help and advice in preparation of this paper at its every step. I gratefully acknowledge the assistance of Dr. M. Hassan, Curator and Assistant Professor of Pathology for his special pathological works with sputum, photography and microphotography and of Mr. Musa Chunara, a student of Medical College for his invaluable help in photographic works. My thanks are due to my clinical assistants Drs. Mohiuddin Ahmed and Shamsul Haque for their close cooperation. I also thank Dr. N. Ali, Principal and Superintendent, Dacca Medical College Hospital for his permission to publish this paper.

RESUMEN

1) Se hace un análisis de los datos clínicos obtenidos en 20 casos de carcinoma bronquiogénico durante 18 meses en el Hospital de la Escuela de Medicina de Dacca en el Pakistan Oriental.

2) Dieciocho de estos casos, provenían de áreas rurales en las que se encuentran pocos caminos asfaltados y automóviles. En la mayoría, no existía el factor de tabaquismo acentuado.

3) La tos, la disnea, el dolor en el pecho o la hemoptisis en una persona de 40 o más años, debe despertar la sospecha del carcinoma bronquiogénico y ser seguida de una investigación pronta y completa.

4) El factor determinante para el diagnóstico, es el estado de alerta por parte del médico, frente a la posibilidad del cáncer.

5) Esta serie demuestra que el carcinoma bronquigénico se encuentra en el Pakistan Oriental con una frecuencia significativa. Como faltan datos anteriores dignos de confianza, la tendencia no pudo determinarse. Un estudio ulterior de esta enfermedad, es por tanto, de extrema importancia en particular, respecto de los factores etiológicos o adyuvantes fuera del uso del cigarrillo o la presencia del esfalto.

RESUME

1) L'auteur analyse les éléments cliniques de vingt cas de cancer bronchique observés pendant 18 mois à l'Hôpital du Collège Médical de Dacca (Pakistan de l'Est).

2) Dix-huit parmi ces cas provenaient de régions rurales, où il y à peu de routes goudronnées et d'automobiles. Dans la plupart de ces cas, les malades n'étaient pas de grands fumeurs.

3) La toux, la dyspnée, les douleurs thoraciques ou l'hémoptysie survenant chez un individu âgé de 40 ans ou davantage, devraient faire suspecter l'existence d'un cancer bronchique et déterminer des investigations rapides et complètes.

4) Il est apparu que ce qui avait avant tout permis le diagnostic, c'était le fait que le médecin eut connaissance de la possibilité du cancer.

5) Cette étude à démontré que le cancer bronchique existe d'une façon particulièrement fréquente dans le Pakistan de l'Est. La possibilité d'une extension actuelle ne peut pas être affirmée en l'absence d'éléments antérieurs valables. C'est pourquoi des études ultérieures sont de la plus haute importance, et elles doivent particulièrement porter sur l'étiologie ou sur les causes favorisantes d'autre nature que le goudron ou l'usage de cigarettes.

Bronchodilator Activity of Three New Drugs in Patients with Pulmonary Emphysema*

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Many therapeutic agents have been employed effectively for the relief of bronchospasm. Preparations in current clinical use have been shown to be more efficacious than older ones, but no single agent has proved entirely satisfactory. Therefore, the present study was undertaken in order to evaluate the bronchodilator properties of three new drugs. As will be demonstrated, extensive preliminary observations showed that only one of these appeared to offer definite indications of therapeutic value. The bronchodilator activity of this drug was then studied in greater detail.

PART I.

Method

Seventeen male patients of average age 59, with intrinsic asthma or hypertrophic emphysema with clinical evidence of associated bronchospasm were studied.

Ventilometric measurements of vital capacity, maximum breathing capacity, volume of deep respiration, and breathing reserve were made with the Collins ventilometer. Although a number of additional tests were employed in this and other studies, these four appeared, in the experience of this laboratory, to provide a simple but reliable clinical measure of lung function. Observations on each subject were made on each of four separate days. The drugs studied, and their dosages, were as follows:

1) Paveril phosphate®** a papaverine analogue - 50 mg.
2) Antrenyl®† anticholinergic - 1.0 mg.
3) Drug 1313,†† adrenergic - 10 mg.

Aminophylline, 0.5 Gm., was separately administered as a basis for comparison.

On each experimental day, the following routine was employed:

1) Slow (5 min.) intravenous injection of normal saline, 10 cc - control.
2) Ten minute interval.
3) Ventilometric measurements.
4) Ten minute rest period.
5) Slow (5 min.) intravenous injection of drug diluted to 10 cc. with normal saline. (The aminophylline was administered in 20 cc. volume as obtained from the ampoule.)

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*From the Veterans Administration Center, Los Angeles, California.

**Supplied through the courtesy of Eli Lilly and Company.

†Diethyl (2 - Hydroxyethyl) Methylammonium Bromide a - phenyl - cyclohexane glycolate, supplied through the courtesy of Ciba Pharmaceutical Products, Inc.

††3, 4-dihydroxy-a-isopropylamino propiophenone hydrobromide, supplied through the courtesy of Sharpe and Dohme, Inc.

TABLE I

EFFECT OF INTRAVENOUS ADMINISTRATION OF DRUGS

Patient	*Vital Capacity (Per cent Change)*				*Volume of Deep Respiration (Per Cent Change)*			
	Aminophylline	Antrenyl	Paveril Phosphate	1313	Aminophylline	Antrenyl	Paveril Phosphate	1313
1	−21	20	12	2	14	18	− 8	−10
2	2	6	1	− 1	9	− 5	−10	−11
3	0	17	− 6	− 2	−14	25	0	8
4	−24	−13	5	29	14	38	13	6
5	0	45	− 7	−18	14	31	0	− 6
6	− 8	28	−11	− 6	− 6	11	0	12
7	− 2	13	24	− 4	20	45	0	− 4
8	6	4	− 6	− 5	23	16	−27	−13
9	13	33	0	10	−10	13	−12	−22
10	9	2	− 2	− 6	0	35	18	13
11	− 6	12	28	3	10	27	46	9
12	− 4	21	− 9	− 9	20	25	9	15
13	14	17	− 4	2	33	11	0	14
14	− 4	0	7	6	14	6	−14	− 4
15	− 4	17	4	− 9	0	23	0	71
16	20	40	20	22	40	33	15	7
17	22	13	5	7	− 7	40	14	− 8
Average	0.8	16.2*	3.6	1.2	10.2*	23.1*	2.6	4.5
S.D.	12.2	14.3	13.8	11.1	14.5	13.0	15.8	19.8

* Statistically significant.

TABLE I (Continued)

EFFECT OF INTRAVENOUS ADMINISTRATION OF DRUGS

Patient	*Maximum Breathing Capacity (Per cent Change)* — Aminophylline	Antrenyl	Paveril Phosphate	1313	*Breathing Reserve (Per cent Change)* — Aminophylline	Antrenyl	Paveril Phosphate	1313
1	20	13	−10	−11	25	37	−20	−17
2	15	26	−13	7	24	42	−11	11
3	7	13	0	0	10	14	0	0
4	0	71	0	−12	−54	244	2	−17
5	55	33	20	16	86	59	39	25
6	8	0	− 8	−12	2	− 4	− 8	−20
7	9	28	8	−14	2	38	−12	−20
8	0	28	−10	−10	− 9	36	−11	−12
9	0	0	20	27	− 3	5	38	29
10	0	25	0	0	−21	43	19	14
11	33	22	6	22	75	30	8	29
12	11	22	− 6	0	10	32	− 6	5
13	9	55	−18	− 7	12	68	−24	− 8
14	0	25	—	− 7	− 7	33	—	− 7
15	11	27	− 9	−32	2	51	−26	−72
16	30	50	7	20	38	228	23	44
17	0	26	36	−15	−10	33	63	−28
Average	12.2*	27.3*	1.4	− 1.6	10.7	41.8*	4.6	− 2.6
S.D.	14.6	17.5	13.9	15.2	32.2	67.1	24.5	26.7

* Statistically significant.

6) Ten minute interval.

7) Ventilometric measurements.

The numerical results of each of these tests were computed for each of the 17 patients after the administration of the placebo control (normal saline) and after the administration of each drug. Differences in the findings after the control and after the drug were expressed as percentage change (Table I).

Results

The largest mean percentage change in vital capacity was produced by the drug antrenyl, which resulted in an improvement of 16.2 per cent over the control figure. The drugs paveril phosphate, 1313, and aminophylline, in contrast to antrenyl, produced changes which were not of statistical significance.

With reference to maximum breathing capacity, antrenyl again gave the greatest mean improvement, 27.3 per cent. Aminophylline produced an improvement of 12.2 per cent. The other two preparations produced effects which were without statistical significance.

Similar results were observed when the mean changes in volume of deep respiration were compared. Antrenyl produced an improvement of 23.1 per cent, aminophylline an improvement of 10.2 per cent, while the other two drugs again produced no significant changes.

Finally, antrenyl produced a striking improvement in the breathing reserve, amounting to 41.8 per cent. The other drugs failed to produce significant change.

The results of these tests of pulmonary function demonstrate that the greatest and most consistent improvement followed the exhibition of antrenyl. Aminophylline gave less marked but still significant improvement. Under the conditions of the experiment, and in the dosages employed, beneficial effects of the other preparations were not remarkable.

Twelve of the 17 patients reported unpleasant dryness of the mouth after the injection of the anti-cholinergic antrenyl, an effect compatible with the pharmacology of the parasympatholytic drugs. Almost all of the subjects reported palpitation, tachycardia, "shakiness or nervousness" following drug 1313. No "side" effects of consequence were noted to result from the administration of aminophylline or paveril phosphate.

When the patients were asked for subjective evaluation of the four substances, there was almost unanimous agreement that antrenyl provided unequivocal and prolonged improvement in breathing. Aminophylline was also felt to be beneficial, but to a lesser degree. The other drugs were without subjective benefit. The oral dryness following antrenyl was severe enough for many of the patients to state that this offset the desirable pulmonary action, so that the over-all subjective effect was unpleasant. In a small group of patients who received this drug by mouth, another undesirable anticholinergic action, namely, difficulty in urination, was a common complaint.

As observed by Dautrebande,[2] the action of drugs administered as aerosols

via the lungs can be limited to the lungs by controlled administration. Therefore, it was decided to administer antrenyl directly to the lung as a nebulized aerosol in the hope that the beneficial pulmonary effect could be obtained with only minimal systemic effects.

PART II.

Method

Observations were made on 45 men in the same age group as the patients studied in the first experiment. These patients clinically were more severely incapacitated than those in the former group. Observations were made before and after the administration of the drug and consisted of ventilometric recording of the expiratory vital capacity, the volume of deep respiration, and the E-E' difference.

The experience gained from studying the first group of patients made it clear that the maximum breathing capacity was too strenuous a procedure for the patients in the second group, all of whom were quite ill. For this reason the maximum breathing capacity, as well as the breathing reserve which depends on it, was not included in the panel of tests.

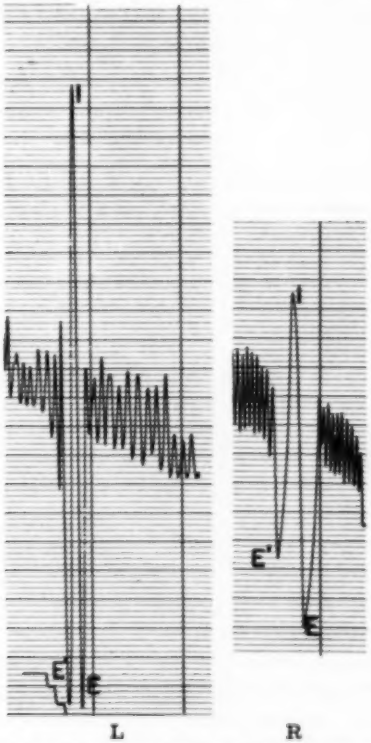

FIGURE 1: Ventilograms showing E-E' differences in normal (L) and emphysematous subjects (R).

The E-E′ difference is the basis of the following recently described[3] simple but reliable ventilographic test of pulmonary function. As shown in Figure 1, it is the difference, stated volumetrically, between the level of maximum expiration, E, attained when expiration is started with the lungs in normal inspiration, and the level of maximum expiration, E′, attained when the next expiration is started with the lungs in maximum inspiration. The normal individual has no difficulty exhaling from any inspiratory position, and E′ will be at or close to the level of E. On the other hand, the individual with bronchospasm "traps" air, so that his ability to exhale is therefore most impaired when he attempts to empty his lungs from the position of maximum inspiration. Hence, the level of E′ will be above the level of E, and consequently, there will be an E-E′ difference. This difference assumes significance when it is expressed as a percentage of the vital capacity, and is normally less than 2 per cent.

Antrenyl (0.5 mg.) was diluted to 1.0 cc. with distilled water and placed in the nebulizer of a Model TV-2P Bennett valve apparatus mounted on an oxygen tank and delivered at a pressure of 20 cm. of water. It was thus administered as a nebulized aerosol over the course of 20 minutes of intermittent positive pressure breathing. This method of drug administration was selected because of its efficacy in introducing therapeutic aerosols to the periphery of lungs having impaired ventilation.[5] Control studies, with the nebulizer containing 1.0 cc. of distilled water, were performed on separate days.

Results

Consistent improvement in pulmonary function resulted from the administration of antrenyl, as demonstrated in Table II. In the 45 patients there were average improvements in volume of deep respiration, vital capacity, and E-E′/VC $\times$ 100 of 21.1 per cent, 16.2 per cent, and 8.2 per cent respectively. With the index of subjective improvement represented on a 0 - 4 plus scale, five reported no benefit, two questionable or 1 plus benefit, eight definite or 2 plus benefit, 21 marked or 3 plus benefit, and nine complete relief or 4 plus benefit. The correlation between subjective and objective findings was crude but unequivocal.

In general, the three indices of pulmonary function employed in this study were consistent. No one test could be singled out as absolutely quantitative, nor could any valid index be derived from pooling the numerical results of the tests. It was therefore concluded that a reasonable over-all estimate of an individual's pulmonary function could be achieved only after the simultaneous consideration of all three tests. As in hepatic disease, a panel of tests seems to provide a better basis for evaluation of function than does any single test.

The control studies in which the patients were observed before and after the administration of distilled water were uniformly and conclusively negative. Equivocal or 1 plus subjective improvement was reported by seven patients. Two of these manifested 2 plus, three 3 plus, and two 4 plus improvement after antrenyl. Definite or 2 plus improvement was

TABLE II

EFFECT OF NEBULIZATION OF ANTRENYL

Patient	Volume of Deep Resp. (Per cent Change)	Vital Capacity (Per cent Change)	$\frac{EE'}{VC} \times 100$ Change	Subjective Estimate of Benefit
1	0	1.1	− 3.2	0
2	12.5	8.4	−14.9	+ + +
3	13.3	1.4	− 4.2	+ + +
4	35.7	28.3	−10.1	+ + +
5	33.3	0	− 7.4	0
6	25.0	32.2	6.6	+ +
7	16.0	30.7	− 2.7	+ + +
8	0	− 5.9	− 9.8	0
9	33.3	31.3	3.6	+ + + +
10	10.0	12.7	0.3	+ +
11	11.1	11.1	−16.2	+ + +
12	25.0	29.8	− 5.7	+ + +
13	17.6	12.6	− 3.9	+ + +
14	7.1	12.5	− 5.6	+ + + +
15	− 6.6	15.0	2.5	+
16	21.4	16.2	− 5.2	+ + +
17	21.4	8.6	−14.6	+ + +
18	12.0	21.0	7.8	+ + + +
19	7.7	2.1	−12.2	+ +
20	9.5	19.4	−16.0	+ + +
21	50.0	13.8	− 5.0	+ + +
22	40.0	2.3	− 6.4	+ +
23	17.6	18.8	−12.4	+ + + +
24	16.7	5.4	−13.8	+ +
25	7.1	12.3	− 3.9	+ +
26	3.8	− 0.9	− 7.0	0
27	5.9	24.6	3.0	+ + +
28	18.7	16.7	−14.6	+ + +
29	46.7	25.0	− 7.9	+ + +
30	11.8	10.8	− 4.7	+ +
31	16.7	30.4	−15.4	+ + + +
32	16.7	11.5	− 8.5	+ + +
33	0	17.3	−13.3	+
34	29.4	14.9	− 6.3	+ + +
35	11.5	− 5.7	−13.1	+ +
36	38.5	15.4	−10.1	+ + +
37	29.4	19.1	−25.0	+ + + +
38	22.2	32.0	−14.2	+ + + +
39	57.1	1.9	−10.0	0
40	21.0	28.0	−10.0	+ + + +
41	25.0	28.0	−10.8	+ + + +
42	16.7	26.1	−20.6	+ + +
43	30.8	13.2	0.2	+ + +
44	6.7	36.5	−28.5	+ + +
45	37.5	28.3	− 1.3	+ + +
Average	21.1*	16.2*	− 8.2*	
S.D.	12.4	10.6	7.5	

* Statistically Significant.

noted by three patients after distilled water. Two of these showed 3 plus, and the third 4 plus improvement after the drug. Thirty-five reported no improvement whatever after distilled water. It is therefore apparent that the positive pressure in itself had no significant effect on lung function.

Comment

In asthma and allied conditions, the relief of bronchospasm is a major therapeutic objective. For this purpose numerous substances have been employed with variable and usually transitory benefit. Since bronchoconstriction is mediated by cholinergic impulses,[4,6] relief should be obtainable by cholinergic blockade. Adrenergic stimulation, which is bronchodilator in effect is also a rational therapeutic procedure. Both avenues of approach have been utilized. Prior to the introduction of potent adrenergic compounds the inhalation of smoke from burning stramonium leaves provided a therapy of sorts, but this at best was of limited value. Cholinergic blockade of slight degree was produced by bringing a small amount of the drug in contact with the effector organ. Adrenergic compounds provided so much greater benefit that the use of stramonium leaves has been generally abandoned. Nevertheless, there was a pharmacologic rationale to their use. The hypodermic administration of epinephrine, being attended by undesirable systemic effects as well as the beneficial bronchodilator action, has largely given way to its administration as a nebulized aerosol. A number of other adrenergic substances are in current use, either by injection or inhalation. Anti-histaminic agents have been disappointing in the treatment of bronchial asthma and other bronchospastic states. This is consistent with experimental observations that the bronchospasm induced by the administration of histamine does not bear the close resemblance to clinical asthma as does the bronchospasm induced by the administration of acetyl choline.[2,4,6]

Although adrenergic stimulation is undoubtedly effective, as experience demonstrates, it might be inferred that this approach, directed toward overcoming a continuing bronchoconstrictor stimulus, is less physiological than one directed toward the actual blocking of the stimulus. It would therefore appear advantageous to attempt to neutralize a cholinergic phenomenon, namely bronchospasm, by cholinergic blockade. Smooth muscle depressants in adequate concentration at the effector organ should be beneficial, but in order to obtain such a concentration it might be necessary to administer so much drug that associated systemic effects would render the drug therapeutically unacceptable. It will be recalled, at any rate, that paveril phosphate, a papaverine analogue, in the dosage employed in Part I of this study, was without measurable effect on pulmonary function.

In attempting to evaluate the efficacy of drugs used for the relief of bronchoconstriction, it is clear that many variables must be taken into account before a valid conclusion can be drawn. For example, it is well known that the degree of bronchospasm present in a given individual may vary spontaneously and widely not only from day to day but from hour to hour. Factors such as weather, emotional state, and infection,

affect the severity of bronchoconstriction to a considerable and usually unpredictable extent. The variability of such influences makes it impossible to establish a true base line of ventilatory function necessary for the comparison of therapeutic agents. Whereas the baseline is subject to wide variation, the level of maximum possible bronchodilatation is relatively constant in any given patient. Consequently, measurements of improvement are directly dependent on the relationship of baseline to maximum levels, i.e., when bronchoconstriction is severe, a greater increase in aeration is possible than when the patient is in remission and already in a relatively favorable state of bronchodilatation. Therefore, in order to avoid reaching untenable deductions concerning the comparative merits of bronchodilator substances, it would be necessary to perform sufficiently numerous tests on sufficiently numerous patients over an entire year. This would minimize seasonal, infectious, atmospheric, and emotional effects.

Because of the aforementioned as well as other difficulties in evaluating so variable a quantity as lung function, many different tests applied singly or in combination have been advocated.[1] The maximum breathing capacity has come to be widely accepted as possibly the most important single test of lung function. Some reservations concerning this test should, however, be borne in mind. In the present series of cases, many patients found that performance of this maneuver was exhausting. They therefore objected to performing it repeatedly. Those patients with the severest respiratory impairment were frequently unable to complete the tests. Because of this and other objections,[3] it was decided not to employ this test in the second group of patients.

In our experience, a panel of three simple tests has provided an apparently reliable reflection of the clinical status. These tests were (1) volume of deep respiration, (2) expiratory vital capacity, and (3) the E-E′ difference. Therefore, in the study of the second group of patients, this panel of tests was substituted for the larger variety of observations made on the first group. Measurements of the first two of these quantities, as detailed in columns one and two of Table II were represented as changes in percentage over control levels induced by the administration of the drug antrenyl. Because control levels were found to be widely variable, it was obvious that percentage changes were far more significant than actual volumetric changes. Column three also denotes percentage change, but the figures were arrived at somewhat differently. Since the value, E-E′/VC x 100, already denotes a percentage, the figures in this column merely represent simple differences in this value induced by drug administration. Because of the nature of this test, a decrease in the figure denotes improvement, or lessening of bronchospasm with its resultant air trapping.

No significant drying effect of this drug was observed in this group of patients, all of whom had copious bronchial secretion. It is to be anticipated, however, that any effective anti-cholinergic preparation will depress secretion. For this reason this drug presumably should not be used in the treatment of bronchial asthma,* but should be reserved for use in

*Currently under investigation.

conditions in which some diminution of the bronchial secretions would not be harmful. Therefore, it should be useful in the treatment of bronchospastic conditions associated with the production of considerable sputum. Our experience supports this view.

SUMMARY

1) From a large number of available tests of pulmonary function, a small group of ventilometric examinations was selected for the purpose of evaluating the effects of three new drugs. This panel of tests is believed to provide a simple but reliable measure of pulmonary function.

2) The effect on pulmonary function of the three drugs administered intravenously was studied in 17 patients having pulmonary disease with associated bronchospasm. One of these drugs (antrenyl[R]) had significant bronchodilator activity.

3) This drug was then administered as a nebulized aerosol to 45 other patients having pulmonary emphysema with varying degrees of bronchospasm. Significant therapeutic benefit was observed in 38 patients.

4) The pharmacology of bronchodilator drugs and the difficulties in estimation of their effects upon pulmonary function are briefly discussed.

The authors are indebted to Mr. Walter N. Holmstrom for his assistance in the performance of this study.

RESUMEN

1) Para valuar los efectos de las nuevas drogas se escogió un pequeño número de exámenes ventilométricos entre el gran número de pruebas de la función pulmonar que existen. Este grupo de pruebas se cree que proporciona una medida sencilla pero digna de confianza de la función pulmonar.

2) El efecto sobre la función pulmonar de las tres drogas administradas intravenosamente fué estudio en diecisiete enfermos con padecimiento pulmonar asociado a broncoespasmo. Una de estas drogas (antrenyl[R]), tiene una actividad definida broncodilatadora.

3) La droga fué administrada en nebulazión de aerosol a otros 45 enfermos con enfisema pulmonar con grados variables de broncoespasmo. Se observó un efecto benéfico en 38 de ellos.

4) Se discuten brevemente la farmacología de los broncodilatadores y las dificultades para apreciar sus efectos sobre la función pulmonar.

RESUME

1) Parmi un nombre important de tests efficaces, les auteurs ont choisi quelques examens de la fonction ventilatoire pour étudier les effets de trois nouveaux produits. Cet ensemble de tests leur à paru réaliser une mesure simple, mais valable, de la fonction pulmonaire.

2) Chez 17 malades atteints d'affections pulmonaires comportant un bronchospasme, les auteurs ont étudié l'action sur la fonction pulmonaire des trois produits, administrés par voie intraveineuse. L'un d'entre eux (l'antrenyl[R]) se montra doué de propriétés bronchodilatatrices nettes.

3) Le produit fut ensuite administré sous forme d'aérosols, à 45 autres malades, atteints d'emphysème pulmonaire, associé à un degré plus ou moins important de bronchospasme. Chez 38 malades, une action thérapeutique heureuse fut observée.

4) Les auteurs discutent rapidement la pharmacologie des produits bronchodilatateurs et la difficulté d'estimer leur effet sur la fonction pulmonaire.

REFERENCES

1 Comroe, J. H.: "Methods in Medical Research," Vol. 2, Sec. II, Year Book Publishers, Inc., Chicago, 1950.
2 Dautrebande, L.: "Aérosols Médicamenteux," Masson et Cie., Paris, 1946.
3 Leslie, A.: "Inspiratory-Expiratory Vital Capacity Test of Pulmonary Function," *Am. J. Med.*, 13:809, 1952.
4 Levinson, L., Beakey, J. F., Bresnick, E. and Segal, M. S.: "Evaluation of Therapeutic Substances Employed for the Relief of Bronchospasm. II. Historical Development and Methods," *Ann. Allergy*, 6:705, 1948.
5 Motley, H. L., Lang, L. P. and Gordon, B.: "Use of Intermittent Positive Pressure Breathing Combined with Nebulization in Pulmonary Disease," *Am. J. Med.*, 5: 853, 1948.
6 Tiffeneau, R. and Beauvallet, M.: "Epreuve de Bronchoconstriction et de Bronchodilatation par Aérosols. Emploi pour le Dépistage, la Mesure et le Controle des Insuffisances Respiratoires Chroniques," *Bull. Acad. de Méd.*, Paris, 129:165, 1945.

The Tuberculous Round Focus in Its Chronic Form*

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Since 1947, with the beginning of the immigration to Israel on a large scale, systematic x-ray examinations were done on immigrants in the reception camps. Now our mass radiographic studies include 350,000 people.

In the first years, 1947-48, the high percentage of cases with active tuberculosis of the lungs was striking (0.8 per cent), and among them we found one particular form of tuberculous lesion of the lung: the tuberculous round focus in its chronic form, a lesion which does not become apparent on clinical examination.

It is the purpose of this paper to deal with it. Those examined were new immigrants to Israel, the majority of whom came at that time from concentration camps in Germany. The minographic films showed small, dense, well defined rounded shadows situated predominantly in the upper lung fields. Their density and their well defined character made them suggestive of fibrotic lesions. But clinical, radiological, and especially bacteriological examinations, carried out over a considerable time, brought us to the conclusion that we were dealing with a chronic round focus, which in the majority of our cases turned out to be the manifestation of an active tuberculous process of latent character.

During 1947-48, 104 cases of round foci of this type were seen on minographic examination of whom 53 were males and 51 were females. More than 50 per cent (59 cases) were 20 to 30 years of age, the usual age groups mostly affected by tuberculous infection.

Of those 104 cases of round foci 85 were single, while 11 showed two foci. One case only showed more than four foci. The total number of round foci recorded was 136 of which 78 were in the right lung and 58 in the left. The most frequent localization was in the upper lung fields, particularly in the second anterior intercostal space, where 72 occurred (31 in the first intercostal space and 13 in the third). The lower lobes were the site of the lesions in 14 cases, of which six were in the apical segments.

One hundred and fourteen (83 per cent) of the lesions showed a typical rounded form, 14 were oval and eight were angular in appearance.

The lesions were relatively small. Sixty-two were 1 to 2 cm. in diameter, 52 were 1 cm., and 22 were larger than 2 cm. In 11 cases deposits of calcium were noted within the foci.

In reading the films a close search was made for additional changes within the lung fields which is important with regard to the pathogenesis of the round foci.

In 75 per cent no additional tuberculous changes were found, either in the vicinity of the round foci, or in other lung fields. In nine cases struc-

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tural intensification was noted in the vicinity of the lesions, assumed to be due to hyperaemia. This finding which was on the border between normal and pathological, deserves particular attention with regard to the clinical evaluation of the case. Clear radiological evidence of additional tuberculous changes in the vicinity of the round foci was found in 24 cases. They were generally of fibrotic character. Six cases showed additional tuberculous lesions in other lung fields, also usually of fibrotic type.

In 28 cases calcified primary complexes were seen in addition to the round foci which is of special significance with regard to the pathogenesis of the round foci.

The radiological finding of a "round-shadow" in the lung has been known to be the manifestation of various pathological processes. One of them is the early tuberculous infiltration ("Fruehinfiltrat") described by Assmann. In its usual form the lesion is ill defined, blurred at the edges, gradually fading off into the surrounding lung field, but it may appear as a well defined rounded lesion.

Another lesion which shows the same appearance on the x-ray film, but differs in its pathology is the round shadow which develops if a cavity turns into a round foci, the so-called "closed type of cavity closure," which has been described by Bobrowitz, Oleneva and Haefliger. The latter author shows 50 cases in which a rounded, well defined focus develops by cavity closure due to closure of the bronchus while the cavity persists. With complete obstruction of the draining bronchus the cavity fills from its walls—the enclosed structure may become inspissated (inspissated cavity).

It therefore follows that various pathological lesions may present themselves in the radiograph as round foci. The x-ray film shows the size and the site of the lesion. Follow-up films over a considerable period of time may reveal changes in the appearance of the foci, permitting a radiological definition of the lesion as to its pathology, but it is impossible to decide from a single film if the round focus is caused by an early infiltration (exudative lesion) or has developed by closure of a cavity.

The early infiltration (Assmann) and the round focus which develops by cavity closure usually manifest themselves by clinical signs. Those affected usually feel ill and consult the physician because of cough, fever, general malaise, etc.; because they have been suffering from acute or subacute illness.

Patients like these are being sent to hospitals for treatment. These presented in this paper felt completely well and had no complaints, except six cases which reported symptoms, but only after close inquiry. The round shadow on the x-ray film of the lung was the only pathological finding, and we had still to define it from the clinical and pathological point of view.

Out of 104 cases, detected during the first few months of systematic minographic examination, 82 remained under our observation and treatment.

Clinical, radiological and bacteriological examinations were done over a considerable period. In 53 cases the time of observation was one to two

years, in 19 cases more than that, 23 from 6 to 12 months, and 10 less than six months.

The radiological examinations showed that in 70 per cent of the cases there was no change in the size or the shape of lesions.

TABLE I

Number of Cases: 104

Male	53	Age:	15-20 years	29
Female	51		20-30 years	59
			30-40 years	12
			40- years	4

The Radiological Findings:

Right side	78	Site:	I Intercostal space	31
Left side	58		II Intercostal space	72
			III Intercostal space	13
			Lower lobe	14
			Apex of lower lobe	6

The Number of Foci in Each Case:

1	35 cases	Shape:	Rounded	114
2	11 cases		Oval	14
3	4 cases		Angular	8
4+	1 case			

Diameter in Centimeters:

Less than 1	52	*Deposits of Calcium*	11
1 to 2	62		
More than 2	22		

Radiological Findings Additional to the Round Foci:

In the vicinity of the foci	24
In other lung fields	6
Calcified primary infiltrate	28
Hyperaemia	9

Results of Observation:

Number of cases	82		
Time of observation in months:			
Less than - 6	10		
6 - 12	23		
12 - 24	30		
More than - 24	19	*Symptoms:*	6 cases

Tuberculosis Bacilli in Cultures of Gastric Washings:

44 positive and 38 negative

Changes of Shape of the Foci:

Increased	5
Decreased	10
Turned into cavity	8

Treatment:

Conservative	63
Pneumothorax	17
Phrenicotomy	2

In a few instances the lesions disappeared by absorption, proof of its recent (exudative) character. Ten showed decrease in size, and five increased during the period of observation. We saw round foci which remained unchanged in their appearance over a long period of time and which were considered inactive, eventually change their shape. They became oval or angular. We have to assume that as long as a focus changes its shape and size it is an active lesion. As mentioned before, a number of round foci showed deposits of calcium.

We noted a number of rounded, dense, homogenous foci which showed small, mostly excentric translucent areas, representing small air-spaces within the foci.

In eight of our cases the round foci turned into cavities without any change in the clinical condition of the patients.

The single film proves only the presence of one of the many forms of a tuberculous lesion in the lungs: the round focus. On account of this single finding we cannot differentiate between a focus which will undergo absorption on the one hand, and a focus which will turn into a cavity on the other. Only serial follow-up examinations over a long period of time may reveal the underlying pathological process which causes the radiological appearance.

In addition to follow-up radiological examinations, systematic clinical investigations were carried out over a long period of time. As mentioned previously, there was nothing in the history of the cases which suggested a tuberculous infection. They did not have symptoms. The general condition of the patients did not give rise to any suspicion of disease. The blood sedimentation rate was normal. The physical examination (percussion and

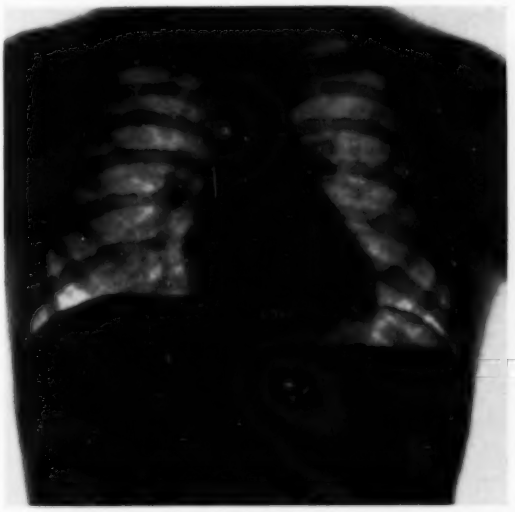

FIGURE 1: A round foci in the right upper lobe (Minograph film).

auscultation) did not reveal any pathological signs. No toxic manifestations were found.

In the absence of any clinical signs we were inclined to consider the lesions described to be of inactive (fibrotic) character.

Bacteriological examinations of the sputum could not be carried out because none of the cases had productive cough. Therefore, systematic bacteriological examinations of gastric washings were started. Serial bacteriological examinations on three or four consecutive days were carried out in each case. The washings were cultured for tubercle bacilli. Out of 82 cases examined this way, 44 (54 per cent) were found to be positive.

Considering the lack of clinical signs those results were unexpected and startling. If in serial radiological examinations signs of activity of the foci were noted, positive bacteriological was usually found. However, in a rather large number of cases in which the round foci remained radiologically unchanged over a long period of time, positive bacteriological findings by gastric lavage were recorded.

The number of colonies of Koch bacilli which grew in cultures, varied. Sometimes, only one or two, again many colonies were found. It happened that in the same patient one series of bacteriological examinations gave negative results while a second series, carried out after two months, turned out to be positive. In bacteriological examinations of this type the evaluation of the results is done by determination of the number of colonies growing in a culture. Though this cannot be looked upon as a mathematical method, the number of colonies grown appears to be an important factor in the evaluation of a case from the clinical point of view. The fact that cultures grown from the gastric juice are found positive for Koch bacilli proves that we deal with a case of active tuberculosis even if there are no other clinical signs apart from the radiological findings of a round focus.

It follows from the above mentioned observations that the clinical evaluation of those 82 cases in which the radiograms showed round foci must differ from that of a round infiltration (Assmann) as well as from the round focus which developed by cavity closure. The latter two lesions which

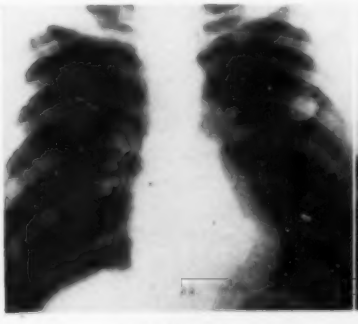

FIGURE 2

FIGURE 3

Figure 2: Round foci in the third intercostal space, left.
Figure 3: Multiple round foci in both upper lobes.

have been clearly defined in the literature, are the manifestation of an acute or subacute disease. The round foci which we have encountered in mass radiographic examinations and which we try to define in this paper may be called "the tuberculous round foci in its chronic form," its main feature being the absence of clinical signs apart from the positive bacteriological finding of Koch bacilli in gastric washings.

Every chronic tuberculous process, in whatever form it may appear, must have been preceeded by an acute stage which may have passed without having been noted at that time. The same applies to the chronic round focus which has been defined in this paper as a clinical entity. The origin must have been one of the forms of an acute tuberculous lesion.

Bobrowitz concludes as a result of his clinical and pathological review of 55 cases that all round foci represent closed cavities. This assumption may be correct with regard to the cases which he describes. However, we believe that there cannot be a single cause only for the development of those round foci. It may be assumed that there are two alternative causes in the development of a round focus: It may either develop from an early round infiltration of exudative-pneumonic character or by closure of a cavity.

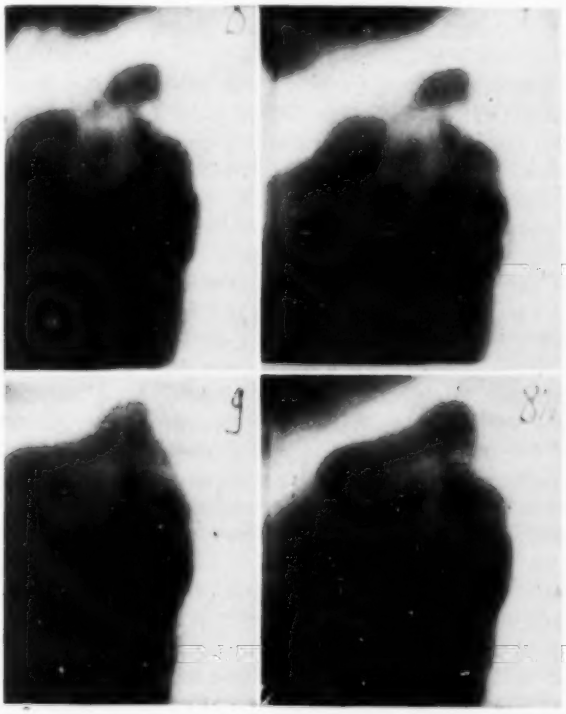

FIGURE 4: Tomogram of round foci with a small translucent area within.

The histological examinations carried out by Assmann in connection with his "Early Round Infiltration" (Freuhinfiltrat) revealed an exudative or caseating lesion surrounded by a fibrotic cover. According to Simmons the round foci have to be considered as the rare forms of early infiltrations which develop by encapsulation of the caseous nucleus which undergoes inspissation. Koch examined histologically eight cases of round foci post mortem. He emphasizes the presence of remnants of elastic fibres within the caseous tissue. Ellinger classified round foci into two forms according to their histological appearance: the caseous and the indurative forms. The results of the pathological examinations done by Oleneva are not uniform. This author describes the round foci on the one hand as lesions surrounded by a fibrotic capsule containing caseous tissue of soft consistency, which may be liquefied, and on the other hand as encapsulated foci with inspissated contents which may contain deposits of calcium. Auerbach and Green and Oleneva have published pathological findings of round foci which were known to have developed by cavity closure ("inspissated cavities"). Auerbach and Green describe their pathological findings as follows: "The foci, on necropsy, have been shown to be spherical bodies of thick caseo-calcified, structureless material enclosed in a dense connective tissue or hyalinized capsule of varied width, demarcated sharply, without surrounding tissue reaction or associated hilar node enlargement."

The pathological findings as reported by Oleneva are similar. She stresses the obliteration of the drainage-bronchus.

The tuberculous round foci in its chronic form may be defined from the pathological point of view as a lesion surrounded by a capsule of connective tissue, the histological architecture of its contents varying according to its pathogenesis. The clinical and the radiological appearance does not reveal the pathogenesis of the lesion. This can be evaluated only by histological examination. If this examination shows that there are remnants of elastic lung structures present within the lesion, then it is highly probable that the round foci developed from a round infiltration.

If elastic fibres are not found within the contents of the round foci it may be assumed that the foci has been preceeded by a cavity and has developed by the closed method of cavity closure. The pathological investigation of the lesion reveals the process which led to the development of the round foci. It may also show signs permitting evaluation regarding the future of the round foci. Such foci may undergo absorption or heal by fibrosis (replacement by connective tissue) and thus become a scar. There may occur caseation of the lesion within its capsule with consecutive liquefaction and so turn it into a cavity or the caseous material may clarify and thus heal by calcification.

In the round foci of the inspissated type ("inspissated cavity") the contents may turn into fibrous tissue. The foci may decrease in size, may change its shape, may become oval or angular, usually triangular, in appearance. This is the indurative stage of the round foci. There is, however, another possibility: the contents may undergo caseation and eventually heal by calcification, or the caseous structures within the foci liquefy, the

draining bronchus opens and the foci turns again into an open cavity.

Some immunological considerations may be indicated. The development of a capsule built of connective tissue surrounding the lesion may be regarded as a manifestation of a local and general resistance. The fact that there was a strikingly small number of negroes among the patients of Bobrowitz in the United States, confirms this opinion, as it is known that the negro are of lesser immunity against tuberculous infection than the white. The cases reported by us were found among immigrants who survived in spite of worse conditions and under nourishment in the German concentration camps. That can only be explained by their natural immunization against the tuberculous infection. There is no doubt, that an overwhelming great number of camp prisoners, lacking this immunity, fell victim to tuberculosis.

It is well known that the round foci may appear as manifestation of the primary tuberculous infection. But it is typical for the primary infiltration that it nearly always involves the regional lymph nodes. We have reviewed our 104 cases in this direction. In none of our cases radiological evidence of involvement of the hilar glands was found. However, in 28 (approximately 30 per cent) of the cases, we did observe in addition to the round foci, calcified lesions in other lung fields, sometimes with calcifications in the respective hilum which we considered to be the calcified primary complex.

These points are suggestive that the chronic tuberculous round foci is to be considered as a manifestation of a post-primary tuberculosis and belongs in the third stage of tuberculosis according to Ranke's classification (the tertiary tuberculosis of the adult).

One question remains to be answered: Is the chronic round foci the result of an exogenous-bronchogenic infection or is it an endogenous-hematogenous infection? Jaffe believes in the hematogenous origin of the round foci. It must be admitted that in certain cases of pulmonary tuberculous lesions it is difficult to decide by the x-ray film if the lesion is of bronchogenous or of hematogenous origin.

But if we take into consideration that in 85 of our 104 cases a single lesion only could be recorded and no other pulmonary tuberculous manifestation was present, the conclusion may be permitted that the round foci are bronchogenous in origin. However, we saw also cases with multiple round foci in both lung fields. In the literature too, cases like those have been reported by Bobrowitz and Albert, but they are rare. It may well be that those are of hematogenous character. We believe that the single round foci will have to be looked upon as being of bronchogenous origin (bronchogenous re-infection).

The prognosis of the chronic round foci has been found to be more favorable than that of the acute or subacute round lesion. As has been pointed out, observation and investigation over a long period of time brought us to the conclusion that the foci under discussion represent a tuberculous lesion of latent character. However, because the foci may become a source of dissemination we have to be cautious with regard to its

prognosis and the patient has to remain under observation over a long period because the latent (closed) foci may turn into an active (open) lesion.

Out of 82 cases which remained under observation and treatment, 63 received conservative treatment, 17 were treated by pneumothorax and two in which the lesion was situated in the lower lobes by phrenicotomy. The comparison of the results of the conservative treatment on the one hand and the collapse therapy on the other showed that there was no difference in the behaviour of those lesions treated by pneumothorax and those which received conservative treatment. That means that collapse therapy did not yield better results than conservative treatment. It may be said that those results could have been anticipated because a lesion surrounded by a fibrotic capsule, cannot be expected to change by collapse therapy. In the cases treated by phrenicotomy no change in the appearance of the round foci was noted. Due to the elevation of the diaphragm after phrenicotomy the foci may change its site, foci in the apical segment of the lower lobe may become hidden behind the shadow of the hilus in the postero-anterior film, but the lateral or oblique film shows it unchanged in size and shape.

According to Oleneva, pneumothorax treatment brought about increased density of the foci. Bobrowitz advocates conservative treatment; only in cases with progressive lesions did he try pneumothorax.

Recent advances of excision surgery in the treatment of tuberculous lesions of the lungs have changed our attitude towards collapse therapy in general. Well known authors express their doubts on the value of the intrapleural pneumothorax even in recent tuberculous lesions, that means doubt in a method which up till recently was considered the method of choice in the treatment of a large group of tuberculous lesions of the lungs. Reports from foremost chest clinics suggest that there has been a growing tendency to reduce also the use of thoracoplasty which for many years has been regarded as the most effective surgical method to achieve a stable collapse of the affected lung. A number of leading chest clinics seem to prefer excision.

It cannot be the task of this paper to express definite views on the value of these methods of treatment. We only wish to stress that close evaluation of the pathological and physiological factors of each individual case will enable us to decide on the way of treatment: resection or collapse therapy.

Regarding the chronic round focus with its defined pathological character it may be said that we do not think that treatment by pneumothorax can be successful. If active treatment becomes necessary, the most promising method of treatment will be resection.

Before considering the differentiation of the lesion from other pulmonary diseases it seems worth while to deal in short with "tuberculoma" of the lung. "Tuberculoma" does not differ in its pathology from the chronic round foci, i.e., a lesion surrounded by a capsule built of connective tissue containing mainly caseous structures which sometimes are partly calcified lying within normal surrounding lung tissue. The term "tuberculoma" is liable to misinterpretation because it gives rise to the association

with a "tumor" while, in fact, we deal with the manifestation of a certain phase of a tuberculous process of the lung. Indeed, the tuberculoma is to be considered as identical in its pathology with the chronic tuberculous round foci.

Not only tuberculous lesions differing in their pathology, but also other diseases of inflammatory, non-specific character may appear in the radiograph as rounded, homogenous, dense shadows. Lobar pneumonia, infiltration of tropical eosinophilia, eosinophylic infiltration (Loeffler), pulmonary lesion of Queensland fever, etc., but they tend to be ill defined and the follow-up of the lesion in connection with the clinical signs usually clarifies the disease.

Differentiation from chronic pulmonary diseases of non-specific character which may also appear on the radiogram as rounded, well-defined shadows will be more difficult. They are: cystic lung tumors, e.g., the hydatid cyst of the lung, benign solid tumors, malignant tumors (carcinoma and sarcoma), primary or metastatic, etc. In a certain number of cases it will be possible to arrive at a correct diagnosis by clinical diagnostic methods. But there remain many cases in which the examination will not yield conclusive results even if all modern clinical and radiological methods of examination are applied. Sometimes, tomography may reveal a central translucent area within the round foci. Though this may point in favor of a tuberculous lesion it cannot exclude a tumor. One should not loose time in cases in which a diagnosis cannot be established in spite of the employment of all modern diagnostic methods. In such cases thoracotomy should be performed. With the great advance of chest surgery the danger of the operation is smaller than that of missing the right time for surgical intervention, e.g., in a malignant tumor.

SUMMARY

In the course of mass-radiographic examinations of new immigrants, carried out in reception camps in Israel, 104 cases were recorded within a short period, showing the radiological finding of a "round-shadow" within the lung. In the early stages of the examinations the lesions were considered of fibrotic (scarring) character.

Clinical, radiological and bacteriological investigations, particularly cultures grown from gastric washings, however, revealed that we were dealing with chronic round foci, which in the majority of cases turned out to be the manifestation of an active tuberculous process of latent character.

A clinical definition of the "tuberculous round focus in its chronic form" has been given and the differential characteristics from the tuberculous round lesion in its acute or subacute form ("early infiltration," Assmann) have been shown, the relationship to the "inspissated cavity" has been discussed.

The pathology of the chronic round foci is assumed to be a lesion surrounded by a capsule of connective tissue containing material of differing histological architecture, in the majority of cases the enclosed materials

being predominantly caseous. The pathogenesis of the lesion is considered to be that of a bronchogenous reinfection.

The treatment is chiefly conservative. If active treatment becomes necessary, resection is preferable to collapse.

The term "round-shadow" is a definition of a radiological appearance which is common to many differing pulmonary diseases. The differential diagnosis of these may be complicated.

RESUMEN

Durante los exámenes de los nuevos inmigrantes en los campos de recepción de Israel, se encontraron en poco tiempo ciento cuatro casos de hallazgos radiológicos de una "mancha redonda" en el pulmón.

Al principio de los exámenes, las lesiones fueron consideradas como de carácter fibroso (cicatriciales).

Sin embargo, las investigaciones clínicas, radiológicas, bacteriológicas y particularmente los cultivos a partir de lavados gástricos, revelaron que se trataba de focos redondos que en la mayoría de los casos resultaron manifestaciones de una tuberculosis activa de carácter latente.

Se da una definición clínica de la "tuberculosis de focos redondos de forma crónica" y las características diferenciales de las lesiones de focos redondos en su forma aguda o subaguda (infiltrado precoz de Assmann) se han demostrado; la relación con la "caverna empastada" se discute.

Se supone que la anatomía patológica del foco redondo crónico, es una lesión rodeada por una cápsula de tejido conectivo que contiene un material de arquitectura histológica varia; siendo en la mayoría de los casos, el material incluído de naturaleza gaseosa.

La patogenia de la lesión se considera que es la reinfección broncógena.

El tratamiento es principalmente conservador. Si se hace necesario un tratamiento activo, la resección es preferible al colapso.

El término "mancha redonda" es una definición de una apariencia radiológica que es común a muchas enfermedades pulmonares. El diagnóstico diferencial de estas enfermedades, puede ser complejo.

RESUME

A l'occasion d'examens radiographiques systématiques, pratiqués pour les nouveaux immigrants dans les camps d'accueils en Israel, l'auteur constata 104 cas pour lesquels existaient une opacité arrondie intra-pulmonaire, et ceci en une courte période d'observation. Dans les premiers moments où furent faits ces examens, il eut tendance à considérer ces lésions comme cicatricielles.

Toutefois, les études cliniques, radiologiques et bactériologiques, et surtout les cultures des tubages gastriques, montrèrent que l'on considéra comme des foyers ronds chroniques des cas qui, dans la majorité, se montrèrent être une manifestation de tuberculose active, mais latente.

L'auteur donne une définition clinique des foyers ronds tuberculeux, dans leur forme chronique, et en montre les caractères différentiels des formes arrondies tuberculeuse, de caractère aigu ou subaigu (infiltrat précoce

d'Assmann). Il discute les relations de ces lésions avec les cavités "épaisses."

L'anatomie pathologique des foyers ronds chroniques se montre être des lésions entourées d'une capsule de tissu conjonctif contenant des éléments d'aspects histologiques divers. Dans la majorité des cas, la partie centrale est constituée par de la matière caséeuse. Au point de vue pathogénique, l'auteur considère que ces lésions sont dues à une réinfection bronchogène.

Le traitement est essentiellement conservateur. Si un traitement actif se montre nécessaire, il faut préférer l'exérèse à la collapsothérapie.

Le terme d'opacités arrondies est une définition radiologique qui peut appartenir à différentes affections pulmonaires. Le diagnostic différentiel peut en être complexe.

REFERENCES

1 Assmann, H.: "Klinische Rontgendiagnostik," F. C. Vogel, Leipzig, 1929.
2 Auerbach, O. and Green, H.: "Pathology of Clinically Healed Tuberculous Cavities," *Am. Rev. Tuberc.*, 42:707, 1940.
3 Berblinger, B.: "Der Schwund Tuberculoser Cavernen," Benno Schwabe and Co., Basel, 1943.
4 Bobrowitz, J. D.: "The Round Pulmonary Tuberculous Focus," *Am. Rev. Tuberc.*, 47:472, 1943.
5 Haefliger, E.: "Die Rückbildung der Caverne über den Rundherd," *Schweiz. Ztschr. Tbs.*, 5:106, 1948.
6 Haeflinger, E.: "Die Form der Tuberculose im Rontgenbild in ihrer Beziehung zu Schub und Rückbildung," Benno Schwabe and Co., Basel 1944.
7 Jaffe, R. H.: "The Pathology of Pulmonary Tuberculosis," Goldberg, B.: "Clinical Tuberculosis," Chapter IV, F. A. Davis Co., Philadelphia 1944.
8 Oleneva, T. N.: "The Round Tuberculous Focus," *Probl. Tuberc.*, 1:10, 1946.

Detection of Hiatus Hernia on 4 x 10 Chest Survey X-ray Films

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Ambroise Pare[32] "anatomized"** the first two reported cases of diaphragmatic hernia, published initially in 1564. Two centuries later, another French surgeon, Petit,[33] described post-mortem findings in hiatus hernia.*** In 1882, Thoma,[41] a pathologist, collected 290 diaphragmatic hernias from the literature: only three of them were para-esophageal. The latter type was thus believed to be very rare.[38]

As early as 1897, fluoroscopy had been considered potentially useful for the detection of diaphragmatic hernia.[37] In 1900, Hirsch[16] and Mertens found the first case, revealed by radiological examination. They reproduced a film of the barium-coated, air-distended stomach, containing a recoiled catheter filled with mercury. It made history, even if the autopsy, performed years later, disclosed an eventration.[2] Eppinger[10] was actually the first to diagnose a hiatus hernia on x-ray films in 1904.

By 1911, 635 diaphragmatic hernias had been published, 11 of which were para-esophageal. Becker[3] contrasted the six cases of diaphragmatic hernia suspected on physical examination (during three centuries) with the 13 cases discovered in the first 15 years of the x-ray era. Early literature, debating the differential diagnosis of hernia vera and relaxation or eventration, has been reviewed by J. M. W. Morrison[27] and Assmann.[2]

At a meeting in Boston (1922), L. B. Morrison[28] and Healy[15] presented 12 hiatus hernias detected during routine x-ray examination of the fundus, originally intended to reveal eventual malignancies. The number was later increased to 32, and finally to 53, which proved that it was not an uncommon finding. In some European textbooks,[43] the credit for this goes to Akerlund,[1] although he arrived at similar conclusions four years later, in 1926.

Today, the high incidence of hiatus hernia is unanimously accepted.[19] It can be seen in 2 to 6 per cent of all barium examinations of the upper G. I. tract.[36] A large number of cases, with literary references covering mainly the last few decades, were published by Kirklin and Hodgson.[21] The condition is often asymptomatic, having been demonstrated in four out of 300 apparently healthy adults.[6]

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**Transcription of French archaism meaning autopsied.

***At an early stage, the difference between the common (sliding) hiatus hernia and the rare (rolling) para-esophageal type consists in the location of the cardio-esophageal junction, which in the former lies above the diaphragm, below it in the latter. At a late stage, due to considerable widening of the hiatal ring, the original condition can seldom be identified, and therefore advanced cases are classified in the first group. In this paper, no attempt has been made to separate the two notions. The term hiatus hernia was introduced in 1922 by L. B. Morrison and Healy of Boston.

The first usable apparatus, for what Manoel de Abreu calls roentgen-photography, was constructed in 1936.

Holfelder and associates[17] used the method for the first time on a large scale. Its popularity can be evaluated from the number of names received: mass (miniature) radiography,[11,25,26,30,42] mass (x-ray) survey,[5,8,14,23] (mass) chest survey,[7,12] routine chest x-ray,[39] photoroentgen,[12] in France radiophotographie,[18] in Germany Schirmbildaufnahme,[17] in Italy schermografia,[24] in Latin America abreugrafia.[9]

It is utilized mainly as a screening procedure for pulmonary tuberculosis. Nonetheless, its value in the detection of non-tuberculous and extrapulmonary conditions has been repeatedly emphasized.[5,8,14,17,24,26,39,42]

A positive diagnosis of hiatus hernia can hardly be made from the postero-anterior chest view alone. Yet, it may be suspected if a supradiaphragmatic fluid level, a gas bubble or a rounded opacity is visualized through the heart shadow, or protruding into either cardiophrenic angle. This finding was described for the first time by Eppinger,[10] and is mentioned in recent textbooks.[34,36,43] It must be differentiated from many similar appearances, such as due to mega-esophagus, esophageal diverticulum, aortic aneurysm, neurofibroma, other varieties of diaphragmatic hernia, ecchinococcus, lower lobe atelectasis, mediastinal abscess or tumor, etc. Nemec[29] has pointed out that in this respect even such trivial changes as dorsal scoliosis or tortuous aorta may prove confusing at times.

Nevertheless, the number of diaphragmatic hernias detected by photoroentgen is insignificant. Often it is totally disregarded,[5,7,9,11,23,24,25,26,30,39] sometimes after 100,000 or more examinations.[4,12,20] When found, the incidence quoted is very low: Trail et al.[42] discovered 13 hernias and eventrations in 250,027 examined; Gould[14] reported 11 diaphragmatic hernias in 442,252 surveyed; Clark et al.,[8] and Holfelder et al.[17] had two cases; Spencer and Schaeffer[40] demonstrated one in 10,661; O'Loughlin[31] one in 24,615. Kohl et al.[22] found only one diaphragmatic hernia in a prenatal chest survey of 4,980 patients. Fifteen years earlier, Rigler and Eneboe[35] had demonstrated 25 hiatus hernias on routine examination of 195 women in the third trimester of pregnancy. The high incidence is probably due

FIGURE 1B

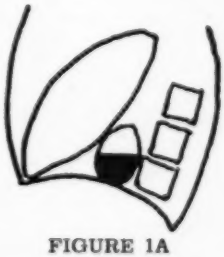

FIGURE 1A

Figure 1A: A hiatus hernia may be suspected from a scout film when a supradiaphragmatic fluid level, a gas bubble, or a rounded opacity is seen through the heart shadow or protruding into either cardiophrenic angle.—*Figure 1B:* The presence of a fluid level between heart and spine is highly suggestive of hiatus hernia. Its positive demonstration requires barium filling.

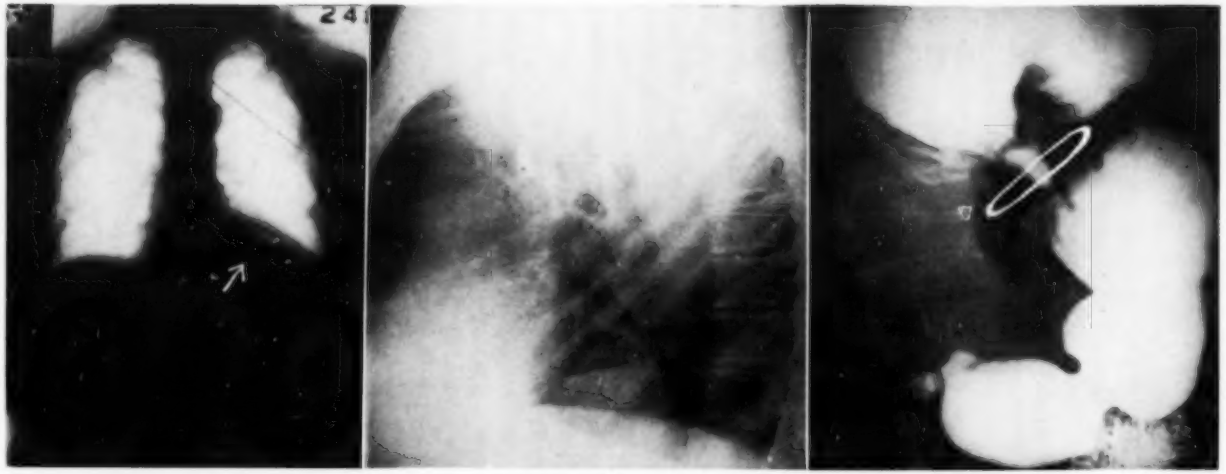

FIGURE 2A FIGURE 2B FIGURE 2C

Figure 2: Case K.A., 57, F, 5'4", 160 lbs.—(A) 4 x 5†: ununited, old left clavicle fracture; left ventricular enlargement; rounded retrocardiac mass with vaguely outlined fluid level to the left of the spine. (B) Left lateral: the stomach fundus is seen protruding above the diaphragm, between heart and spine. (C) Right anterior oblique in prone Trendelenburg reveals a recoiled body, with gastric folds widely spread through the hiatus.

†The photofluorograms are reproduced from positive contact prints for better visualization of density changes in the cardiac opacity.

to intra-abdominal pressure changes, because seven out of 10 proved cases showed no evidence of herniation on recheck after delivery.

Modern tuberculosis control in mental institutions requires routine chest x-ray film on admission, as well as biannual survey of patients and employees alike. In this hospital, 4 x 10 (stereo) is used for this purpose, questionable and pathologic findings being rechecked on 14 x 17 plates. The various wards are x-rayed by rotation, which provides a continuous flow of films to the reading room, rather than heavy piles twice yearly.

At first, an obvious hiatus hernia was discovered in the survey. As a consequence, more attention was paid to the retrocardiac shadow on the miniature films, and soon cases began to accumulate at the rate of one every eight to 10 days. To the date of this writing, 21 have been demonstrated. Three other patients, two of them males, were unable to cooperate for the examination; their resistiveness prevented filling of the stomach with barium by catheter, a last resort in several cases.

The patient population fluctuates around 4,200. No percentages shall be calculated, because of (a) the relatively fast turnover of patients,† (b) the addition of new cases at each survey, and (c) the concentration of older age groups in the hospital's patients which raises the apparent insidence, since hiatus hernia is more frequent after the fifth decade. Only eight of the 21 proved cases were males. This may be due to the prevalence of older females in our mental, as well as in the general, population.

Altogether, our figures are in agreement with the findings of Froman,[13] who demonstrated 58 diaphragmatic hernias over a period of several years in a hospital for the mentally ill with a census twice as large as this institution.

In many of our cases, a lateral chest view, taken after a carbonated drink, revealed a circular shadow with fluid level, located between heart and spine, which we like to consider a highly presumptive sign for the presence of hiatus hernia. Positive proof was obtained routinely in supine Trendelenburg, during barium meal, with or without Valsalva maneuvers. Left and right oblique exposures were taken routinely, to rule out a short esophagus, to evaluate the extent of the herniation, and to visualize eventual recoils of the body.

The reasons for overlooking hiatus hernia on plain chest films (4 x 10 or 14 x 17) are manyfold. They shall be discussed under three convenient headings: the hernia, the film, and the examiner.

In the observation princeps,[33] no adhesions had formed between the herniated organs and the diaphragm. In the light of our present knowledge, this seems to be the rule, rather than the exception. Reduction of the hernia can often be induced by simple maneuvers such as walking, deep breathing, leaning forward, taking a warm drink, etc. Prerequisite for such a "pendular" condition is a wide rent in the diaphragm, or a relaxed esophageal ring. The latter case seems to be quite frequent in the older

†Two died, one was released on family care, one was transferred to another institution, and two additional cases have been discovered among those admitted within the last three months, ending April 30, 1953.

FIGURE 3A FIGURE 3B FIGURE 3C

Figure 3: Case I. A., 76, F, 5'1", 140 lbs.—(A) 4 x 5: increased density of soft tissues of neck (goiter); rounded widening of the upper mediastinum; prominent aortic knob; double cardiac contour. (B) Right lateral: retrocardiac supradiaphragmatic fluid level with gas bubble. (C) Postero-anterior view in erect position, after ingestion of thick barium, demonstrates a (pendulous) pulsion diverticulum, emerging at the pharyngo-esophageal junction; the supradiaphragmatic fundus is also visualized.

age groups, particularly in overweight individuals, in which instance hiatal "insufficiency" or "incompetence" would be a suitable name. Obviously, the chest film must be negative, if the stomach was in the abdomen during the exposure. This is why the retrocardiac opacity may alternately appear and disappear on successive views. Two cases were added to our list because the ward was surveyed shortly after lunch. Perhaps the ingestion of a carbonated drink, just before the exposure, would increase the number of hiatus hernias detected on routine (admission) chest x-ray films.

The photoroentgen film has a blue sensitive, high speed emulsion, and retains good tonal qualities and definition, but it can only reproduce what it "sees" on the large sized grains of the screen. Moreover, developing in the x-ray solution will emphasize the contrast, with the intent to "bring out" eventual soft pulmonary shadows, assumed to occur often in early tuberculosis. As a result, the range of densities is shortened, which again decreases the chances of detecting variations in the cardiac opacity. On the other hand, in the overweight, excessive secondary radiation will deposit enough silver to hide everything behind a gray curtain. This goes also for the 14 x 17, in which case a higher penetration, a Bucky or even a stationary grid, might be of help in revealing retrocardiac shadows. However, until recently, anything over 70 KVP was considered unsuitable for chest diagnosis. While high voltage techniques for regular chest films are presently on trial in several places, it is worth mentioning that in 1948, Jaubert de Beaujeu[18] had suggested it for roentgenphotography. He used 180 KVP, 200 MA at 120 cm. focus-screen distance, the exposures being 0.25 to 0.3 seconds for adults, 0.1 to 0.15 seconds for children. Contrary to previous assumptions, if the MAS are kept within reasonable limits, the soft shadows will not be "burned out".

Chest people have sometimes a tendency to limit their evaluation of the thorax film to what is more or less strictly connected with pulmonary disease. A wider outlook is in order. The radiolucent area in that upper rib giving away the diagnosis of a rounded apical mass; the fractured rib labeling a pleural reaction as traumatic; the subcutaneous emphysema proving a bronchial leak in cases of trauma without demonstrable pneumothorax; these are but a few instances in which chest diagnosis will benefit from careful inspection of every highlight and every density, however remote and apparently insignificant. Furthermore, one seldom sees something that he is not prepared to find. Of course, a stomach projected over either lung field will hardly be overlooked, but those are exceptions. The average sized hernia may not be discovered, unless constant alertness is maintained for the possible detection of retrocardiac shadows. After some practice, it becomes part of the routine, like the upward glimpse, intended to avoid the omission of a clavicle fracture.

There is a tendency to multiply the surveys in the population, and to introduce miniature chest films in the admission routine of most general hospitals. Thus, the radiologist and the chest man are in a position to detect more and more cases of hiatus hernia. The reward for such endeavor is under circumstances gratifying. The internist can be provided

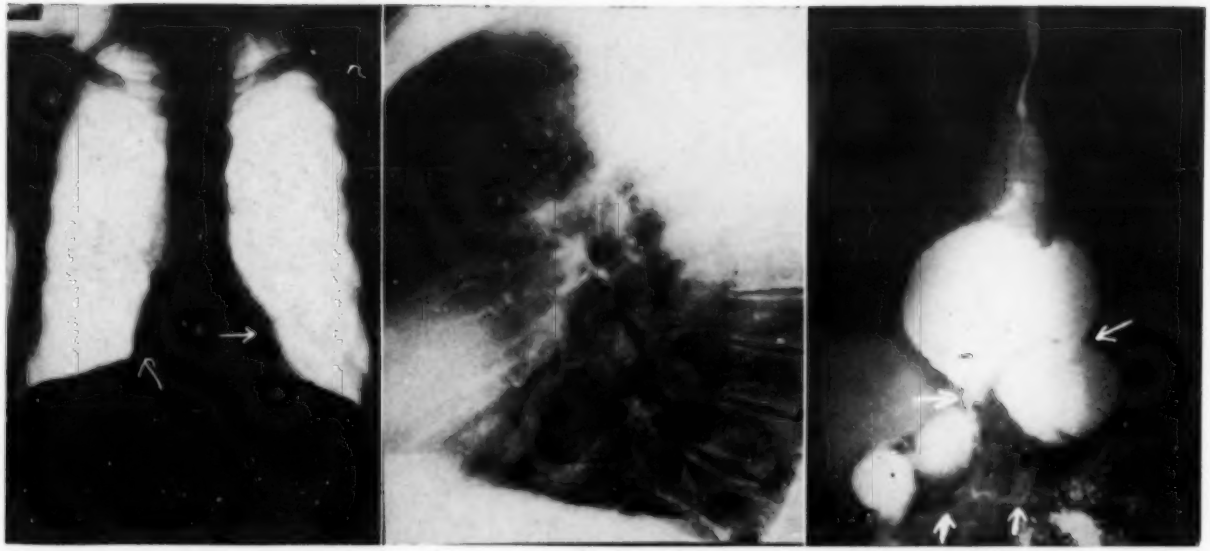

FIGURE 4A FIGURE 4B FIGURE 4C

Figure 4: Case W. R., 69, M, 5'7", 150 lbs.—(A) 4 x 5: generalized emphysema; mildly tortuous aorta; retrocardiac gas bubble, without fluid level, to the right of the spine; retrocardiac opacity, without evidence of gas, to the left of the spine. (B) Left lateral: the usual fluid level in the lower mediastinum. (C) Postero-anterior view in supine Trendelenburg: large hiatus hernia containing most of the body of the stomach; double contrast visualization of the greater curvature (rudimentary Hampton technique). The herniated portion of the stomach is recoiled, biloculated, and twisted. Food is often retained in the proximal segment (projecting to left of spine), and gas was trapped in the distal portion (to right of spine): maybe the unusual appearance on the photoroentgen could in itself suggest a volvulus.

with a valid alternate diagnosis, when the precordial pain of an old gentleman means four to six weeks (coronary) bed rest. Similarly, the surgeon may be warned that his lady-patient will probably continue to complain of postprandial distress even after removal of the gallbladder.

SUMMARY

Hiatus hernia, frequently due to hiatal relaxation or incompetence, is relatively common in the pyknic individual over 50. Three cases are illustrated, these being selected from 21 proved hiatus hernias, detected on 4 x 10 chest survey among 4,200 patients of a hospital for the mentally ill.

On a plain chest view (4 x 5 or 14 x 17), the presence of a hiatus hernia may be presumed when a supradiaphragmatic fluid level, a gas bubble, or a rounded opacity is visualized through the heart shadow, or protruding into either cardiophrenic angle. Sometimes, the condition cannot be suspected from the scout film; the reasons for this are analyzed.

Suggestions for a more frequent detection of hiatus hernia from 4 x 5 or 14 x 17 plates include: (a) ingestion of a carbonated drink before exposure of routine chest x-rays, (b) high KVP technique, and (c) alertness for variations in the density of the cardiac shadow.

RESUMEN

La hernia del hiatus, frecuentemente debida a relajamiento hiatal o a insuficiencia del hiatus, es relativamente común en los sujetos pícnicos de más de 50 años. Se presentan tres casos ilustrativos, se leccionados entre 21 casos demostrados de hernia del hiatus, descubiertos en la investigación con película de 4 x 10, entre 4,200 enfermos de un hospital de enfermos mentales.

En una película sencilla de 4 x 5 o de 14 x 17, la presencia de hernia del hiatus, puede presumirse cuando se observa un nivel líquido supradifragmático, una burbuja de gas, o una opacidad redonda a través de la sombra del corazón o haciendo saliente en cualquiera de los ángulos cardiofrénicos. A veces la anomalía no puede sospecharse por la película de ordinaria investigación; se examinan las razones para que esto ocurra.

Sugestiones para que se logre más a menudo el descubrimiento: en películas de 4 x 5 y 14 x 17 incluyen: (a) ingestión de una bebida bicarbonatada antes de tomar la película de rutina; (b) Alto kilovoltaje y estar alerta de los cambios de densidad de la imagen cardíaca.

RESUME

La hernie à travers le hiatus oesophagien, causée surtout par le replâchement ou l'insuffisance du hiatus, est relativement fréquente chez les sujets pycniques après 50 ans. Trois observations illustrées ont été choisies parmi 21 cas prouvés, découverts pendant l'examen systématique du thorax (radiophotographie sur films 4 x 10 inches) de 4200 malades dans un asile d'aliénés.

On peut présumer l'existence d'une telle hernie lorsqu'on trouve sur le cliché standard (4 x 5 ou 14 x 17 in.) un niveau de liquide, une bulle gazeuse

ou une opacité arrondie, projetés au-dessus du diaphragms et visibles à travers l'ombre du coeur, parfois même saillant dans un des angles cardio-phréniques. Quelquefois, le premier film ne permet pas de soupçonner une hernie; les raisons en sont discutées.

Pour augmenter le nombre des cas de hernie du hiatus découverts sur des radiographies 4 x 5 ou 14 x 17 in., l'auteur suggère (a) l'ingestion d'une boisson gazeuse avant la prise du cliché, (b) l'usage d'une technique à haut kilovoltage, et (c) être à l'alerte pour les variations de densité de l'ombre cardiaque.

REFERENCES

1 Akerlund, A.: "Hernia diaphragmatica Hiatus Oesophagei vom anatomischen und roentgenologischen Gesichtspunkt," *Acta radiol.*, 6:3, 1926.
2 Assmann, H.: "Klinische Roentgendiagnostik der inneren Erkrankungen," 3rd ed., F. C. W. Vogel, Leipzig, 1924 (pp. 381-390).
3 Becker, T.: "Roentgenuntersuchungen bei Hernia und Eventratio diaphragmatica. Drei neue Faelle ein Beitrag zur klinischen Diagnose," *Fortschr. a. d. Geb. d. Roentgenstrahlen*, 17:183, 1911.
4 Bew, D. F., Tilney, R. W. Jr. and Maher, W. E. J.: "Review of 283,225 Chest Photofluorograms at U. S. Naval Personnel Separation Center, Lido Beach," *U. S. Nav. M. Bull.*, 47:749, 1947.
5 Boucot, K. R. and Cooper, D. A.: "Critical Evaluation of Mass Roentgen Surveys," *J.A.M.A.*, 142:1255, 1950.
6 Brick, I. B. and Amory, H. I.: "Incidence of Hiatus Hernia in Patients Without Symptoms," *Arch. Surg.*, 60:1045, 1950.
7 Burnett, J. W. and Tice, G. M.: "Mass Chest Survey at University of Kansas Medical Center Outpatient Dispensary," *J. Kansas M. Soc.*, 49:19, 1948.
8 Clark, D., Temple, C. W. and Allen, K. D. A.: "Diagnosis of Pulmonary Lesions Discovered by Mass Roentgenographic Survey," *J.A.M.A.*, 143:943, 1950.
9 Cunha de Abreu, J.: "A abreugrafia na profilaxia das doencas cardio-pulmonares," *Gaz. med. port.* (Lisboa), 2:1065, 1949.
10 Eppinger, H.: "Beitrag zur Roentgendiagnostik und pathologischen Anatomie einer Hernia diaphragmatica paraoesophagea," *Zeitschr. f. Heilkunde (Int. Med.)*, 25:364, 1904.
11 Evans, A. G.: "Results of Mass Radiograph of R. A. F. Ex-prisoners-of-war from Germany," *Brit. M. J.*, 1:914, 1946.
12 Fine, A. and Steinhausen, T. B.: "Experiences with Photoroentgen Method in Chest Surveys; Analysis of 156,000 Examinations," *Ohio State M. J.*, 41:709, 1945.
13 Froman, A.: Personal communication.
14 Gould, D. M.: "Non-Tuberculous Lesions Found in Mass X-ray Surveys," *J.A.M.A.*, 127:753, 1945.
15 Healy, T. R.: "Symptoms Observed in Fifty-Three Cases of Non-Traumatic Diaphragmatic Hernia," *Am. J. Roentgen.*, 13:266, 1925.
16 Hirsch, C.: "Zur klinischen Diagnose der Zwerchfellhernie," *Muenchen. med. Wchschr.*, 47:996, 1900.
17 Holfelder, H. and Benner, F.: "Atlas des Roentgenreihenbildes des Brustraumes auf Grund der Auswertung von ueber 900,000 Roentgenreihenschirmbildern," G. Thieme, Leipzig, 1939.
18 Jaubert de Beaujeu, A.: "La radiophotographie a tres haut voltage," *J. de radiol. et d'electrol.*, 27:352, 1946.
19 Jenkinson, E. L. and Roberts, E. W.: "Lesions of Diaphragm," *Am. J. Roentgen.*, 38:584, 1937.
20 Kinsey, F. R.: "Pathologic Chest Findings in 100,000 Consecutive Examinations of Army Separatees," *Bull. U. S. Army M. Dept.*, 9:1051, 1949.
21 Kirklin, B. R. and Hodgson, J. R.: "Roentgenologic Characteristics of Diaphragmatic Hernia," *Am. J. Roentgen.*, 58:77, 1947.
22 Kohl, S. G., Kaltreider, D. F. and Davidson, C. W.: "Unknown Intrathoracic Complications Discovered by Routine Prenatal Chest Roentgenography," *Bull. School Med. Univ. Maryland*, 37:28, 1952.
23 Krasnitz, A.: "Mass X-ray Survey in Burlington County," *J. M. Soc. New Jersey*, 44:493, 1947.
24 Luzzatti, G.: "L'errore nel l'interpretazione dell'imagine schermografica," *Arch. tisiol. (sez. scient.)*, 5:32, 1950.
25 McLachlan, I. M.: "Mass Radiography; Review of First Year's Working," *J. Roy. San. Inst.*, 66:1, 1946.

26 Maxwell, J., Kerley, P. and Paxon, T.: "Discussion on Non-Tuberculous Conditions Revealed by Mass Radiography," *Proc. Roy. Soc. Med.*, 42:1039, 1949.
27 Morrison, J. M. W.: "Elevation of the Diaphragm. Unilateral Phrenic Paralysis. A Radiological Study, With Special Reference to the Differential Diagnosis (Conclusion)," *Arch. Radiol. and Electrotherap.*, 28:111, 1923.
28 Morrison, L. B.: "Diaphragmatic Hernia of Fundus of Stomach Through the Esophageal Hiatus," *J.A.M.A.*, 84:161, 1925.
29 Nemec, S. S.: "Differential Diagnosis of Retrocardiac Shadows," *Radiology*, 50: 174, 1948.
30 Nightingale, J. A.: "Chest Abnormalities Detected by Miniature Radiography," *J. Roy. Army M. Corps*, 98:224, 1952.
31 O'Loughlin, B. J.: "Study of 24,615 Seperation Chest Roentgenograms," *Radiology*, 48:389, 1947.
32 Paré, A.: "Oevvres," Ed. princeps. Gabriel Buon, Paris, 1575; x, 32 (p. 387).
33 Petit, L. J.: "Traité des maladies chirurgicales, et des opérations qui leur conviennent," P. Fr. Didot, Jr., Paris, 1774 (t. 2, p. 261-264).
34 Rabin, C. B.: "Radiology of the Chest," v. 1, chap. 3 in "Diagnostic Roentgenology," R. Golden, Ed. Williams & Wilkins, Baltimore, 1952 (p. 192 S).
35 Rigler, L. G. and Eneboe, J. B.: "Incidence of Hiatus Hernia in Pregnant Women and Its Significance," *J. Thoracic Surg.*, 4:262, 1935.
36 Ritvo, M.: "Chest X-ray Diagnosis," Lea & Febiger, Philadelphia, 1951 (p. 329).
37 Rosenfeld, G.: "Die Diagnostik innerer Krankheiten mittels Roentgenstrahlen," Bergmann, Wiesbaden, 1897 (p. 26).
38 Schwalbe, E.: "Beobachtung eines Falles von Hernia diaphragmatica vera," *Centralbl. f. allg. Path. u. path. Anat.*, 11:262, 1900.
39 Slattery, R. V., Beadenkopf, W. G. and Loosli, C. G.: "Nature of Lesions Encountered in Routine Chest X-rays," *J. Lab. Clin. Med.*, 36:617, 1950.
40 Spencer, J. and Schaeffer, J. H.: "Analysis of the Chest Survey Program at the Maine Medical Center," *J. Maine M. A.*, 42:264, 1951.
41 Thoma, R.: "Vier Faelle von Hernia diaphragmatica," *Virchow's Arch. f. path. Anat.*, 88:515, 1882.
42 Trail, R. R. et al.: "Mass Miniature Radiography in R. A. F.; Report on 250,027 Consecutive Examinations of R. A. F. and W. A. A. F. Personnel," *Brit. J. Tuberc.*, 38:116, 1944.
43 Zuppinger, A.: "Das Zwerchfell" in "Lehrbuch der Roentgendiagnostik," H. R. Schinz et al., Ed., 5th ed., G. Thieme, Leipzig, 1952 (Lieferung 6, p. 2580).

An X-ray Study of Spontaneous Pneumothorax Due to Cancer Metastases to the Lungs*

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Introduction

The purpose of this article is to call attention to the possibility of spontaneous pneumothorax occurring secondary to pulmonary metastases. Besides reporting seven new cases showing this condition, we emphasize that one of the tumors involved was a carcinoma. The nine cases we have been able to locate in previous writings are summarized in Table I.

Case Reports

Case 1: This 34 year old man had a leiomyosarcoma of the rectum. He had been treated by surgery and radiation therapy for this tumor prior to admission to Memorial Center. The admission chest x-ray examination revealed nodular cancer metastases to the lungs (Figure 1). He was given a course of x-radiation of the rectum and was discharged. He was re-admitted four months later complaining of severe shortness of breath and pain in the chest of several days duration. X-ray examination of the chest one day following admission revealed bilateral hydropneumothorax with multiple pulmonary metastases (Figure 2). The pulmonary nodules had increased in size and number since the examination six months previously. Bilateral under-water deflation was performed, and there was immediate improvement in his condition. Follow-up chest x-ray films one day later revealed re-expansion of both lungs and regression of the pleural effusion. He was discharged after seven days as improved.

Case 2: A nine year old white male was admitted to Memorial Center with a diagnosis of Ewing's tumor of the sacrum. A chest x-ray film six days before admission revealed bilateral pneumothorax and pulmonary metastases (Figure 3). He had received x-ray therapy to his chest and sacrum elsewhere for six weeks, continuing up to the time of admission. Treatments were discontinued because of the pneumothorax. Interval chest x-ray film examination up to the time of his discharge three weeks after admission showed gradual improvement in the chest lesions and pneumothorax, presumably due to the previous treatment (Figure 4). He was re-admitted four months after the first admission complaining of shortness of breath and chest pain. The chest x-ray film examination showed bilateral pleural effusion and increase in the size of the pulmonary metastases. There was gradual improvement, however, in the patient's condition on medical treatment. He was discharged in three weeks. At the final admission two weeks later, x-ray films of the chest revealed further increase in the pulmonary metastases and pleural effusion. Repeated thoracentesis was unsuccessful for the most part. Only small amounts of bloody fluid could be obtained. He remained moderately dyspneic and slightly cyanotic. The child was placed in an oxygen tent. There was little improvement, and he died nine days after admission. No autopsy was obtained.

Case 3: This 55 year old white male was admitted to Memorial Center with complaints of shortness of breath, cough, and fatigue of one month duration. X-ray film examination of the chest nine days prior to admission had revealed

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right hydropneumothorax (Figure 5). Also noted was a density at the right apex which had been present for six months. Thoracentesis was performed, and a bloody pleural fluid was obtained. Papanicalaou studies of the effusion were reported as Class III-IV. Right thoracotomy was performed, and partial decortication and biopsy done. The pathological diagnosis was: "metastatic adenocarcinoma; the possibility that this lesion is primary in the lung is remote." Subsequent studies were unable to uncover the primary lesion. The patient made a somewhat slow recovery and was discharged two months later.

Case 4: This 20 year old white female was admitted to the Memorial Center following right nephrectomy at another hospital 23 months previously. The tumor of the right kidney was reported as a myosarcoma of the adult Wilms' type. Several months following the nephrectomy, she noted shortness of breath and x-ray film of the chest three months after operation revealed pneumothorax with nearly complete collapse of the left lung. A small effusion was also present (Figure 6). Three months later, the left lung had re-expanded completely, but the right lung was about 50 per cent collapsed (Figure 7). During this period, there was progressive development of fine patchy nodular densities throughout both lungs. Later, both lungs were expanded; multiple film studies of the chest from this time to the date of her admission, revealed increase in the nodular densities throughout both lungs. Also there was a small area of pneumothorax in the left apex and left base. This became larger over a period of two months. The opinion was that the chest findings represented a lymphatic type of cancer metastases, with the areas of pneumothorax being secondary. She was discharged after a few weeks and had two episodes of spontaneous pneumothorax. Three months later she was re-admitted, and several procedures were carried out in an attempt to expand the lungs. X-ray film at the time of the second admission revealed 25 per cent to 30 per cent pneumothorax on the right, and 20 per cent on the left (Figure 8). There was gradual re-expansion of the lungs. Films made 10 days after admission revealed bilateral pneumothorax again, and she appeared worse. Thoracotomy tubes were placed in the chest. She was subsequently placed in an oxygen tent and received a blood transfusion. Four days before death, cortisone was commenced. Final x-ray film of the chest revealed some re-expansion of the lungs. She died two months after her second admission.

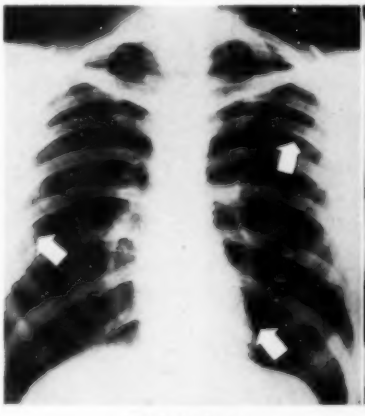

FIGURE 1

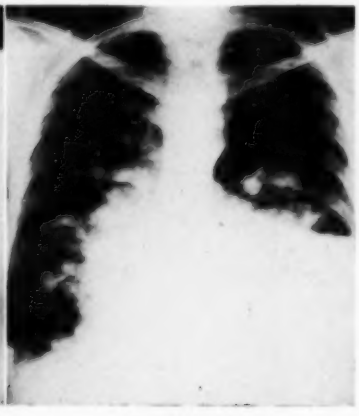

FIGURE 2

Case 1, Figure 1: Small metastatic nodules in both lungs.
Figure 2: Bilateral hydropneumothorax. Increase in size and number of pulmonary metastases.

FIGURE 3 FIGURE 4 FIGURE 5

Case 2, Figure 3: Bilateral pneumothorax.
Figure 4: Interval improvement of pneumothorax.
Case 3, Figure 5: Density in right apex and right hydropneumothorax.

TABLE I

AUTHOR	NO. OF CASES	PRIMARY TUMOR	ROENTGEN FINDINGS	AUTOPSY FINDINGS
Thornton and Bigelow, 1944	1	Fibrosarcoma of the hand	Unilateral pneumothorax with extensive pulmonary metastases.	Bilateral pneumothorax, both lungs collapsed and solid with firm tumor nodules.
	1	Osteogenic sarcoma of the femur	Left pneumothorax, right hydrothorax with pulmonary metastases.	Both lungs contain tumor nodules up to 3 cm. in diameter. Many nodules necrotic, injected air escaped through a necrotic nodule.
Lodmell and Capps, 1949	1	Osteogenic sarcoma of the tibia	Bilateral pneumothorax with multiple pulmonary metastases.	Necrotic tumor nodules eroding the pleura. The large necrotic pleural nodules show complete infarct-like necrosis with extensive hemorrhage into and around the tumor.
	1	Fibrosarcoma of the soft tissue of the neck	Bilateral pneumothorax with extensive pulmonary metastases.	Massive tumor invasion of both lungs with cystic degeneration; tumor well vascularized with tendency to surround and invade the vessels.
	1	Retroperitoneal angiosarcoma	Unilateral pneumothorax with numerous metastatic nodules in both lungs.	Tension pneumothorax on left. Tumor had grown from parenchymatous nodules through the pleura to invade the lateral chest wall. One tumor nodule was perforated to form a fistula.
Christmann, Schoposwki and Deschamps, 1950	1	Endothelioma of calcaneus	Unilateral pneumothorax with bilateral pulmonary metastases.	None.
Shaw, 1951	1	Leiomyosarcoma of the uterus	Bilateral pneumothorax with pulmonary metastases	Bilateral pneumothorax; multiple tumor masses throughout both lungs. The degree of differentiation of the leiomyosarcoma was extremely variable. Necrosis was widespread.
Leigh and Thompson, 1951	1	Osteogenic sarcoma of the tibia	Unilateral pneumothorax with bilateral pulmonary metastases.	None.
	1	Osteogenic sarcoma of the humerus	Unilateral pneumothorax with bilateral pulmonary metastases.	None.

FIGURE 6 FIGURE 7 FIGURE 8

Case 4, Figure 6: Left pneumothorax three months following surgery.
Figure 7: Right pneumothorax three months later.
Figure 8: Bilateral pneumothorax at second admission.

At necropsy the lungs together weighed 1,300 gms. The pleural surfaces were markedly thickened. On external examination the lungs were studded everywhere with tumor nodules measuring from 1 to 5 mm. in size. The nodules were so numerous and so diffusely scattered as to suggest lymphangitic spread. The bronchial tree was not remarkable. The lungs were rather poorly distended with air. The sectioned surface of the parenchymal tissue showed tiny cystic structures which were thought to be dilated air sacs. These tiny cystic structures were everywhere in intimate relationship to the small tumor nodules. No pneumonia was found.

On microscopic examination the pleura was covered by a layer of granulation tissue, fibrin, and fibropurulent exudate. Tumor infiltrated the subpleural tissue and alveolar walls, and to a greater degree in the right lung. The tumor was composed of spindle cells with irregular hyperchromatic nuclei showing occasional mitoses. Tumor masses were usually small with indistinct outlines and having an intimately associated capillary network. In some infiltrated areas, there was hemorrhage and clumps of pigment-filled macrophages; in other areas lung tissue was normal or atelectatic. There was diffuse spread of tumor in the lungs with formation of varied sized cystic spaces.

The final pathological diagnosis was mysarcoma of the right kidney with metastases to lungs and hilar lymph nodes.

Case 5: This 16 year old white male was admitted to Memorial Center with a diagnosis of tumor of the sacrum. Aspiration biopsy five days later established a diagnosis of Ewing's tumor. He had previously received two courses of x-ray therapy at another hospital.

X-ray film revealed a destructive lesion of the fourth sacral segment and widespread bilateral pulmonary metastases (Figure 9). Beginning six days after admission, he received another course of radiation. Follow-up x-ray films one month after admission showed interval improvement in the sacrum and lungs. Three months after admission, x-ray films revealed extensive bilateral pulmonary and mediastinal metastases with pneumothorax on the left side (Figure 10). Also noted was a pathological fracture of the neck of the left femur. In an attempt to relieve

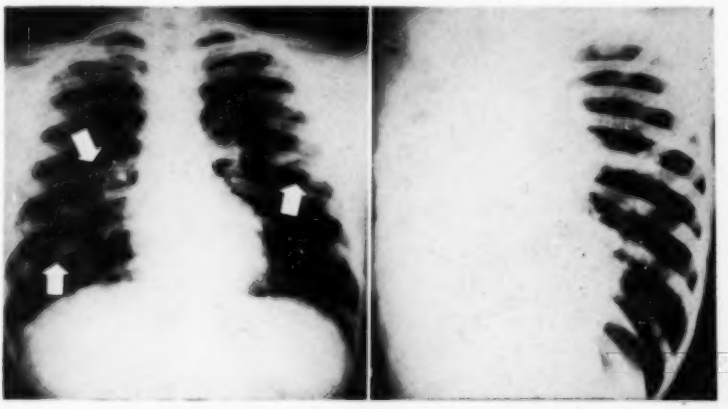

FIGURE 9 FIGURE 10

Case 5, Figure 9: Bilateral pulmonary metastases.

Figure 10: Lateral decubitus film. Three months later extensive pulmonary metastases and left pneumothorax. Note large pleural nodule in left lower chest

the cardiorespiratory embarrassment, 300 to 400 cc. of air were removed on several occasions, but the air reaccumulated. His course rapidly worsened with death five and one-half months after admission.

On necropsy the lungs presented a remarkable appearance. The parenchyma was almost entirely replaced by masses of soft gray white homogeneous tumor tissue occurring in nodules varying in size from 1 cm. to 5 or 6 cm. in diameter. A few of the nodules showed hemorrhagic zones, but the large bulk of the tumor was neither necrotic nor hemorrhagic. The bronchi were not encroached upon. The uninvolved portion of the left lung was completely atelectatic. Uninvolved portions of the right lung showed congestion and edema. The parietal pleuras were extensively involved by tumor similar in appearance to that described in the lung. Large tumor nodules studded the diaphragmatic surfaces of both pleural cavities and were found lying on the pleura in para-vertebral position.

The anatomical diagnosis was endothelial myeloma of the sacrum with metastases to the left femur (pathological fracture of left femur) to mediastinum, lungs and visceral and parietal pleurae; pneumothorax, left, massive atelectasis of left lung and cardiac dilatation.

Case 6: This 17 year old boy was admitted to Memorial Center with a diagnosis of "fibrosarcoma" of the left thigh. One week following admission, left hip disarticulation was performed, and the pathological diagnosis was rhabdomysarcoma. His postoperative course was uneventful, and he was discharged about two weeks following admission. He was observed periodically, and seven months following the operation, he had soft tissue metastases of the scalp as well as an osteolytic lesion in the calvarium. A chest x-ray film at this time revealed multiple pulmonary nodules measuring up to 3 cm. in diameter and there was about a 5 per cent pneumothorax on the right (Figure 11). Chest films at the time of surgery had been negative for pulmonary metastases. Chest x-ray films six weeks after the appearance of the pneumothorax showed it to still be present on the right but to a lesser degree. The pulmonary metastatic nodules were increased in size and number. He was admitted to the hospital and his condition became quite critical, and he died suddenly five days after admission.

Necropsy revealed both pleural cavities to contain about 200 cc. of thick hemor-

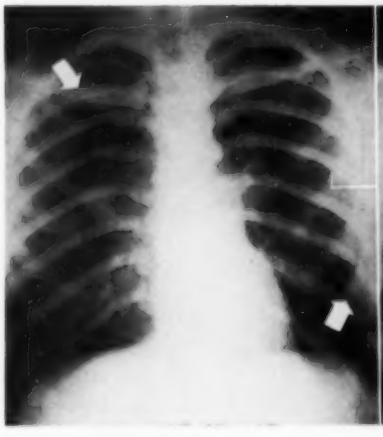

FIGURE 11

FIGURE 12

Case 6, Fig. 11: Five per cent pneumothorax on right and pulmonary metastases.
Case 7, Fig. 12: Massive collapse on the right and bilateral pulmonary metastases.

rhagic fluid, rich with fibrin. The parietal and visceral pleura sowed irregular, diffuse fibrous adhesions throughout. Multiple tumor nodules protruded from the visceral pleural surface. The bronchi and vessels showed occasional compression and stenosis by the multiple metastatic tumors in the lung parenchyma. The largest tumor nodule measured about 8 cm. in diameter. It was grayish-white in color, soft, and showed central hemorrhagic necrosis. Throughout both lungs there were varying sized nodules, many of which were situated in the subpleural area. The pathological diagnosis was rhabdomyosarcoma metastatic to lungs and bone.

Case 7: This nine year old girl was admitted to Memorial Center with the chief complaint of pain and swelling of the left leg for four months. X-ray films of the leg on admission revealed osteogenic sarcoma of the left tibia. A chest x-ray film at this time was normal. The pathological report was that of osteogenic sarcoma. She received intensive radiotherapy to the left tibia. A mid-thigh amputation was performed and her postoperative course was essentially uneventful.

She remained well until about three months following amputation when a chest x-ray film revealed lesions throughout both lung fields. She was admitted to the hospital three weeks later because of hemoptysis, pain in the chest and progressive dyspnea. X-ray film of the chest revealed right hydropneumothorax with considerable collapse of the right lung. The bilateral metastatic nodules had increased in size (Figure 12). The following day there was some re-expansion of the right lung, but the left lung now showed a 40 per cent collapse. Bilateral intercostal drainage was performed, and she showed marked but temporary improvement. Interval chest films over the next two weeks showed some improvement in the degree of pneumothorax, but the nodules were increasing rapidly, the right lung being nearly replaced by tumor tissue. Her breathing became more labored, and she lapsed into come and died five and one-half weeks following admission. No autopsy was obtained.

Discussion

During the past 10 years at Memorial Center, there have been at least seven instances of spontaneous pneumothorax associated with and apparently due to pulmonary metastases. While it is evident that sarcoma is the most frequent cause of pneumothorax, the occurrence of a metastatic carcinoma associated with a spontaneous pneumothorax indicates that metastases other than sarcoma may be a cause. Neither we nor the pathological laboratories at Memorial Center can offer an explanation as to why sarcoma metastases, rather than carcinoma metastases should bring about this condition with significantly greater frequency.

Thornton and Bigelow[1] are of the opinion that the pneumothorax associated with pulmonary metastasis is caused by actual rupture of a necrotic tumor nodule causing a communication between a bronchus and the pleural cavity. They were able to demonstrate this in their second case. Because necrosis seems to be a prominent feature in these secondary tumor nodules, it might be expected that perforation into the pleural cavity should occur more frequently. However, these authors feel that since metastatic tumors usually do not involve a bronchus, this fact may explain the rather uncommon complication of pneumothorax in cases of pulmonary metastases.

Lodmell and Capps[2] believe that there is no single explanation which can be given for spontaneous pneumothorax in all cases of pulmonary metas-

tases. They believe that a bronchopleural fistula resulting from necrosis of a subpleural nodule is not necessarily always the manner in which pneumothorax occurs. For instance, in one of their cases there were necrotic tumor nodules extending through the pleura, but no fistulous tract was demonstrated. Their opinion is that due to the absence of inflammatory changes, the necrosis was of recent origin, more recent in fact than the pneumothorax. The pneumothorax had been present for several weeks. In their first two cases, the tumor nodules at the lung periphery had produced bronchiolar obstruction. Through a ball-valve action over distention occurred, and tearing of the walls permitted air to pass along the interlobular septa to the pleura with the formation of blebs. Rupture of the blebs subsequently occurred. Several other factors considered by Lodmell and Capps were the alteration of the tensile strength of connective tissue by the rapidly growing tumor, as well as invasion and obliteration of blood vessels causing edema and poor nourishment of the tissues with subsequent weakening. They also considered the effect of muscular effort of patients who are ambulatory as a possible factor in producing greater intrabronchial and intrathoracic pressures. Christmann, Schoposwki and Deschamps[3] believe that the pneumothorax in their case of Ewing's tumor of the calcaneus was a result of necrosis of tumor nodules following radiotherapy to the lungs. In a case reported by Shaw,[4] the pneumothorax appeared to be due to the formation of a bronchopleural fistula following necrosis of a subpleural nodule. Leigh and Thompson[5] have reported two cases of osteogenic sarcoma with pulmonary metastases and pneumothorax. They offer no explanation for the occurrence of the pneumothorax, since there was no autopsy material in either case. Their second case is of special interest because the pneumothorax preceded visible metastatic deposits in the lungs by nearly two months.

Because the first case of this series is still alive, we can only speculate as to the possible mechanism producing the pneumothorax. The rapid increase in bilateral metastatic pulmonary disease may have led to necrosis of some of the nodules, resulting in the pneumothorax. This patient was ambulatory at the time of the pneumothorax. The case of the Ewing's tumor presented many subpleural nodules. Though there were many which were not necrotic, necrosis of a single deposit could have been the causative factor of the pneumothorax. Necrotic areas were also present in the instance of metastatic adenocarcinoma of the lung. Necrosis of tumor nodules and rupture of subpleural blebs were the possible causative factors in the case of myosarcoma of the kidney. The tumor infiltrated the alveolar walls, but was also associated with numerous "cystic" structures. Central hemorrhagic necrosis of tumor nodules in the visceral pleura with numerous nodules in the subpleural area dominated the findings in the last patient with rhabdomyosarcoma.

SUMMARY

Seven patients showing spontaneous pneumothorax associated with metastases have been described. These include four metastatic sarcomas,

two of Ewing's tumor, and one of metastatic carcinoma. The metastatic carcinoma is the first instance that we know of in which a metastasis other than sarcoma has been the cause of spontaneous pneumothorax.

While one must concede that spontaneous pneumothorax can occur with any type of pulmonary metastasis, there is a distinct preponderance for sarcoma metastasis to be associated with this condition. The exact mechanism of the pneumothorax formation is not clear, but the weight of evidence suggests that most episodes are due to necrosis of tumor nodules with the production of bronchopleural fistulae.

RESUMEN

Se han descrito siete casos de neumotórax espontáneo asociado a metástasis. Tales casos incluyen sarcomas metastásicos, dos de tumor de Ewing y uno de carcinoma metastásico. El carcinoma metastásico referido, es el primer caso que conocemos en que es la causa de un neumotórax espontáneo aparte de los casos de sarcoma.

Si bien debemos conceder que el neumotórax espontáneo, puede ocurrir con cualquier forma de metástasis, hay cierta predilección para que ocurran más en el sarcoma. No está claro el mecanismo de la aparición del neumotórax espontáneo, pero la evidencia gravita en favor de que la mayoría se deben a necrosis de nódulos tumorales con producción de fístulas broncopleurales.

RESUME

Les auteurs décrivent les observations de sept malades atteints de pneumothorax spontanés, au cours de métastases cancéreuses. Il s'agit de quatre sarcomes métastatiques, de deux tumeurs d'Ewing, et d'un carcinome métastatique. Le carcinome métastatique est le premier exemple qu'ils connaissent dans lequel une métastase non sarcomateuse à été la cause d'un pneumothorax spontané.

Bien qu'on puisse concevoir qu'un pneumothorax spontané soit possible avec toutes les catégories de métastases pulmonaires; il y à une prépondérance nette du sarcome métastatique. Le mécanisme exact de la constitution du pneumothorax n'est pas clair, mais il semble évident que le plupart des épisodes sont attribuables à la nécrose des nodules cancéreux, avec production de fistules bronchopleurales.

REFERENCES

1 Thornton, T. F. and Bigelow, R. R.: "Pneumothorax Due to Metastatic Sarcoma," *Arch. Path.*, 37:334, 1944.

2 Lodmell, E. A. and Capps, S. C.: "Spontaneous Pneumothorax Associated with Metastatic Sarcomas," *Radiology*, 52:88, 1949.

3 Christmann, F. E., Schoposwki, F. and Deschamps, H. Jr.: "Spontaneous Pneumothorax in Pulmonary Metastases of Endothelioma of the Calcaneum," *Dia Medica*, 22:58, 1950.

4 Shaw, A. B.: "Spontaneous Pneumothorax from Secondary Sarcoma of Lung," *Brit. M. J.*, 1:278, 1951.

5 Leigh, T. F. and Thompson, E. A.: "Pulmonary Metastatic Sarcoma with Associated Pneumothorax," *Am. J. Roent. and Rad. Ther.*, 66:900, 1951.

The Successful Treatment of Diseases of the Respiratory Tract by Continuous Postural Drainage and the Prevention Thereby of Recurrent and Chronic Affections

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In a previous paper (1949) it was postulated that most cases of recurrent or chronic inflammatory disease of the lungs and paranasal sinuses originate in the incomplete resolution of an initial lesion whether bronchitis, bronchopneumonia, or sinusitis; that these diseases progress largely by exacerbations, frequently brought about by intercurrent infections.

This initial lesion frequently occurs in infancy or early childhood but it may occur not uncommonly in later childhood or in adolescence or with a diminishing frequency of incidence at any period during the rest of life.

In many cases recovery from this lesion may appear complete and no ill health may ensue until this permanent damage is aggravated by a fresh infection of adequate severity at some later period.

It was suggested tha tthe main cause of this lesion is the persistence of a residuum of accumulated secretions brought about by physical difficulties in effecting their adequate evacuation, difficulties which appear to have arisen through the evolutionary assumption of the erect posture by man.

The objective of continuous postural drainage is to facilitate the evacuation of these secretions through the action of gravity by placing the main outlet, whether bronchus or ostium in a dependent position; this again should permit the better functioning of the physiological means of evacuation, viz. ciliary and peristaltic action assisted by the act of coughing when necessary.

Di Rienzo (1950) has recently given us a graphic picture of coughing as a dynamic act expelling air or secretions by a high speed peristaltic wave. He moreover noted that bronchial branches which have been destroyed by infection or modified by bronchiectasis do not expel their contents during cough having lost their dynamic properties.

In chronic bronchitis the persistent irritation of the mucous membrane of the bronchi and of the underlying layers leads in the course of time, to thickening of the bronchial walls with increase of the fibrous tissue in the outer layers (Davidson, 1935).

When this condition is further advanced, as in bronchiectasis, this infiltration of the bronchial walls by fibrous tissue may reach an extreme degree.

The retention of excessive secretions, it is suggested, is an important factor in bringing about these changes as well as tending to produce areas of collapse, whether great or small, through their viscid character in

certain cases even in tenuous layers, as in a case described of obstruction of a main bronchus by a film of mucus no thicker than a soap bubble causing post-operative collapse which was promptly relieved by sucking away the mucus (Hirschfeld, 1951). Such factors, occurring in a progressive inflammatory disease will tend to cause progressive interference with both ciliary activity and the so-called bronchial dynamic action, leading up to the complete loss of the power of evacuation of the bronchial contents which may be seen in bronchiectasis.

If we may judge by the results achieved, continuous postural drainage can do much to prevent such a course of events.

Scope of Application: The late H. P. Nelson (1934) devised a bed supporting a hinged frame on which the patient lay prone, with the trunk and lower limbs on either slope, for the continuous drainage of lung abscess and bronchiectasis. However such a posture tends to become irksome and does not permit any turning or change of position which is usually so necessary, at intervals, to facilitate drainage of the various ramifications of the affected segmental bronchi. Also the elevation at an angle of 20 or 30 degrees, as Nelson suggested, is unnecessarily high.

Lack of lasting results following the accepted vertical intermittent method of posturing, even when carried out to the utmost limit of endurance, viz. sessions of an hour, in one case, led me to follow Nelson's suggestion for continuous treatment on the same patient then aged 49, but on a modified plan with the foot of the bed raised 18 inches, with most satisfactory results. This woman, now aged 67, is still sleeping on the same slope with firm support. Prior to treatment she had had repeated attacks of pleurisy and pneumonitis following a nearly fatal attack of double pneumonia, eight years earlier. She was never free from a most distressing and practically non-productive cough. A bronchogram revealed saccular bronchiectasis of both lower lobes and auscultation disclosed râles extending from both bases to the mid-scapular level. Modified râles are still audible over the same area but she has been free from all symptoms for many years with the exception of 12 months when she went without her posture and had a partial relapse. She has been enjoying normal activity and better health than ever in her life before.

After achieving considerable success in bronchiectasis it seemed to be

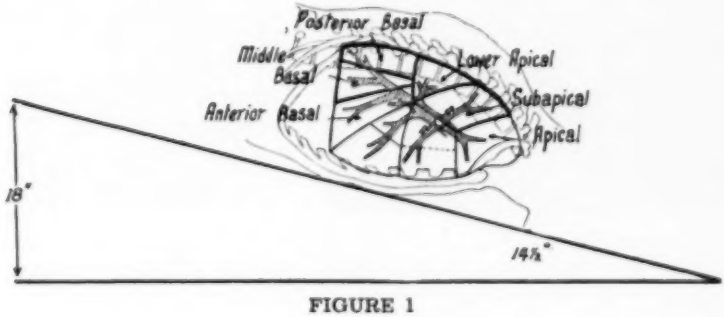

FIGURE 1

FIGURE 2

FIGURE 3

Figure 2: Male, aged 45 years. Frequent and persistent bronchitis from early childhood. Pneumonia and pleurisy when 14 years old; febrile pleurisy every year since. Rheumatic fever when 20 years of age. Increasing productive cough and shortness of breath on exertion. Nutrition always poor. Constant insomnia. — *On Examination.* Pigeon breast. Palpable diastolic thrill at apex with accentuation of first sound and slight presystolic rumble. ***X-ray film of Chest*** showed prominent auricular curve. Thickened pleura at left base and bronchiectasis at both bases suggested. Reported back after sleeping four years on the slope. Had no recurrence of the pleurisy pain whatever until recently when pain returned after he had slept for three weeks on flat bed owing to discomfort from auditory meatitis. Pain was promptly relieved by raising the bed. — *On Examination.* Heart sounds clear. No thrill palpable. ***X-ray film of Chest*** showed marked improvement and clearing of soft densities at bases but honeycomb marking clearly shown at both bases. Auricular curve less prominent. — *Figure 3:* Female, aged 21 years. When first seen seven years ago she complained of asthma and severe productive cough for five years past following measles. Asthma attacks increasing in frequency and severity up to three in a week. Frequent doses of adrenalin needed. For two days after each attack she would bring up one-fourth cupful of thick yellow sputum each day. She became free from all symptoms after three years posture despite regular employment in clothing factory. Married two years later and had a moderate attack following neglect of posture for the fortnight's honeymoon. Now has only fleeting tightness in the chest and practically no cough or sputum despite heavy domestic work and much worry. Still posturing.

only reasonable to apply the same treatment to its potential precursors, to cases of unresolved pneumonia (so-called), recurrent bronchopneumonia or pneumonitis, chronic or recurrent bronchitis, basal bronchitis, recurrent pleurisy, usually basal, to all similar stages intermediate in the development of pulmonary fibrosis and bronchiectasis, as first visualized by Riviere (1923) and Nobécourt (1924) and later by Davidson (1935), in the hope of at least delaying and if possible arresting and preventing further progress towards such serious irreversible conditions, if indeed such development had not already taken place.

The final step was to secure by the same method more certain resolution of the original lesions with a view to preventing the development of the recurrent and chronic conditions already mentioned. Opportunities for this were, however, by this time limited by early retirement from active hospital staffs but the results of the few cases recorded have been 100 per cent and lasting without any known recurrence. The six cases of bronchopneumonia averaging 60 years of age, were all severe, with cyanosis and respiratory distress and with one exception had no benefit from antibiotics, as they occurred before their general use. The six acute cases grouped as Br. 3 had less severe pneumonia or pneumonitis. There were also two cases of abscess already mentioned in an earlier communication, both with severe and increasing toxaemia, one of three weeks duration, sub-apical with a fluid level, and the other of the middle lobe, of seven weeks duration. Both responded promptly and permanently to suitable posturing, and have now been free from any chest symptom for more than 10 years.

The fact that bronchitis and sinusitis frequently precede or complicate asthma and hay fever led to a trial in both of these latter conditions with excellent and lasting results in practically all cases in which full and continued co-operation of the patient and relatives could be secured.

Method of Application: "The Bed": The essential need is to avoid sagging of the mattress. The thorax and head should be inclined at approximately the same angle as the bed itself. Any deviation from this cardinal principle will tend to vitiate results. Reinforcement with 5-ply boarding, etc., is often necessary. Most persons, even the most elderly, soon learn to prefer a firm bed but strong inner spring mattresses can be most comfortable and quite adequate.

The Pillow: If the sinuses are involved no pillow should be used, or, if essential for comfort, a very low one chiefly supporting the neck and allowing the head to definitely slope downwards. However most patients after experience with and without a pillow prefer to discard it. Children never need pillows.

A firm buffer will usually be needed across the top of the bed to prevent discomfort from any contact with the head; a soft pillow should not be used for this purpose as it may tend to work under the head and interfere with its slope.

A loose mattress may need to be secured to the foot of the bed to prevent it sliding down and curling up at the bottom. If any tendency to slide downwards causes real discomfort the shoulders may be kept in place by

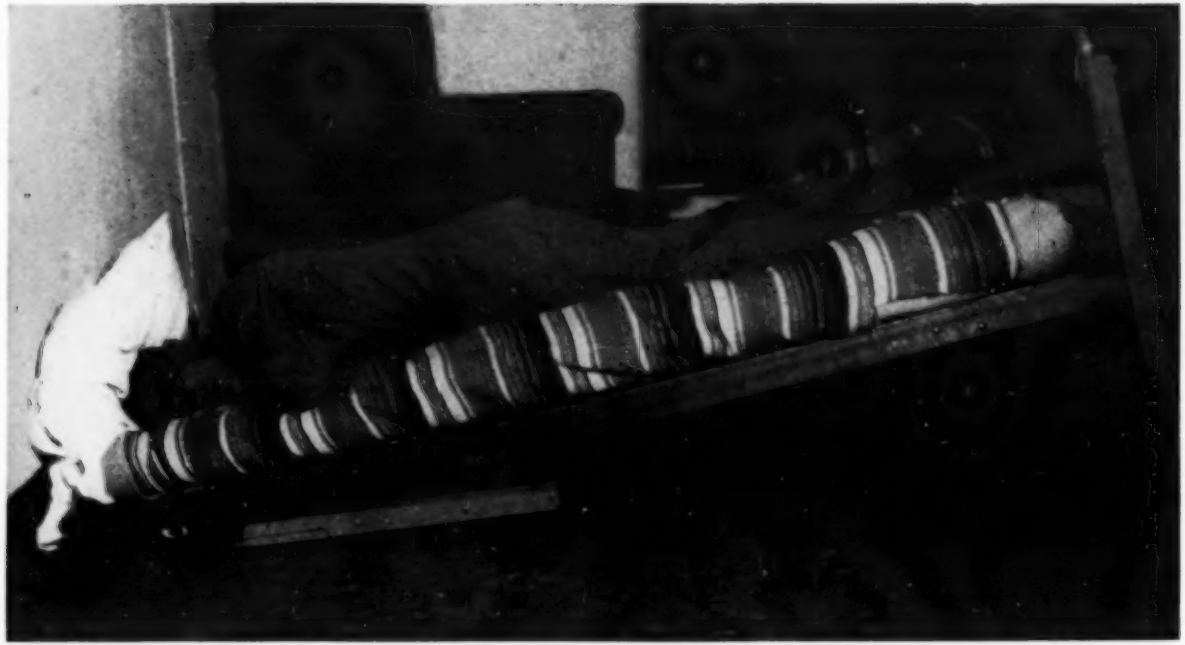

FIGURE 4: This patient commenced treatment six years ago when aged 29 years. He had suffered from persistent colds ever since birth and from asthma and bronchitis since he was four years old. The attacks gradually became more severe, one every two to three weeks when he would bring up daily a cupful of yellow sputum. He was never entirely free from asthma at night. After sleeping on the slope for two years he reported that his general health had improved remarkably, enabling him to enjoy life to the fullest, a new experience. Any slight tightness in the chest at night or on sharp exertion would be promptly removed with a single whiff from an atomiser. After six years he reported that he was still improving and had never missed a day's work as draughtsman in the Post Office despite much overtime.

a strong pair of men's braces fastened to the foot of the bed. Some such arrangement of shoulder straps is suitable for young children with a waist band and side bands loosely attached to the sides of the bed or cot to permit adequate turning from side to side but preventing any cross-bed position being adopted.

Elevation: An elevation of the foot of the bed by 18 inches, that is at an angle of 14½ degrees (Figure 1) has been found the best for most chest cases. Persons with viscid sputum may prefer an elevation of from 19 to 22 inches at least as a temporary measure.

For sinusitis without any chest complication, 15 to 16 inches will be found adequate. If circumstances do not permit a raising of the bed a strictly horizontal posture with no pillow may allow fair drainage but a definite slope is always far more effective.

Rationale of Posture Adopted: Utilizing Brock's (1947) diagrams (Figure 1) the outline of the segments most commonly involved has been accentuated and the direction of the main draining bronchi is indicated with the patient at an angle of approximately 14½ degrees.

Lying on alternate breasts choosing the less affected side for the longer periods, is the best routine posture to adopt and most patients find it quite comfortable.

In this way the posterior basal and lower apical segments are well drained together with contiguous portions of the middle basal and subapical segments. Turning on the back with the necessary inclination to the appropriate side will drain the middle lobe and the lingula also the more anterior basal bronchi when these are known to be affected. Apart from these indications it is well to warn patients to keep off the back as much as possible so as to break what is a fairly normal habit. Once they

FIGURE 5: Male child, aged six years, seen only once two and a half years ago. Severe bronchitis with asthma five or six times every year since an attack of bronchopneumonia when six weeks old. Attacks becoming more severe. During the first three months of sleeping on the sloping bed he had two further severe attacks necessitating adrenalin injections, but the bed had sagged. Improved promptly on changing to new bed and had only one attack, a mild one, a year later and has had none of any kind in the last 18 months. Greatly improved in general health.

are on the slope however they often state that they get choked up if they lie on their backs and are glad to avoid doing so.

Results

The fact to be borne in mind in assessing the value of these results is that a large proportion of patients did not return after the first consultation although always urged to do so. Consequently there was no opportunity in these cases of making any adjustments that were frequently necessary towards securing the best results. As the patient's home was rarely visited the only real check was by photographs which few provided. An increasing but still limited number of family physicians are becoming co-operative and encouraging the treatment but may fail to ensure its adequacy. The amazing fact is that the results are as good as they are, and moreover they are constantly improving.

Excellent results in all groups follow early application of the treatment. The longer the main symptoms have lasted the greater the damage and the less satisfactory the results.

Only 56 cases of undoubted bronchiectasis have been included in Grade Br. 4, but judging by history and suggestive radiological and physical signs there would be many of those classed as Br. 3 which would have a greater or lesser degree of bronchiectasis as well as many asthmatic and tuberculous cases. Of these 56 cases 23 per cent progressed to grade +4 and 55 per cent to grade +3.

Out of all cases (599) a considerable number of the 42.6 per cent graded +3 (greatly improved) in this progress are well on their way to grade +4 (completely and lasting symptomatic relief). This observation is supported by the greatly increased proportion of cases graded +4 in the recent assessment, viz 44.4 per cent of 599 patients in 1952 as against 19.7 per cent of 416 patients in 1948.

All cases are examined radiologically as a routine.

It needs to be emphasized that excluding the cases of tuberculosis and the few cases of recent origin 86 per cent of all others were in the category of severe and refractory cases.

If the treatment was used for cough alone it would be abundantly justified. A perpetual distressing cough which may have lasted a lifetime will often be dramatically and permanently relieved even though in some cases little or no extra sputum may be produced. Likewise also all other bronchitic symptoms, the wheezing and tightness, the pain due to recurrent pleurisy or pleural irritation, which is generally basal, the progressively increasing shortness of breath on exertion, the hours of nocturnal orthopnoea can all be strikingly relieved and in most cases abolished completely.

Above all, the constant succession of severe colds, the bouts of recurrent chest and sinus inflammation to which the progressive nature of the chronic disease is essentially due, are rapidly relieved and in a large proportion of cases removed altogether. Complete relief of cough and other symptoms however must depend on two essential conditions, firstly there

must be no obstruction to the draining bronchus due to stenosis or kinking from fibrous contraction, pressure by fibrous bands or new growth, etc. Secondly the posture adopted must be the most suitable with due respect to the areas involved, and the period of application must be adequate.

In all cases of extensive bronchiectasis especially those with frequently recurrent pneumonitis or with gross pansinusitis, and in all the most severe cases of asthma, especially when complicated with bronchiectasis or severe sinus disease continuous night and day posture, with short breaks for meals, will be advisable for weeks or months and may be continued for years with great benefit. In any case there should always be extra posturing for as long as possible during the day; this is applicable to all patients as a general principle.

Children often produce sputum for the first time on coughing when under treatment instead of being forced to retch it up, if they produce any at all.

In a previous paper (1949) the results of treatment in all decades were given, showing, as might be expected that the younger the patient the better the result.

So far, out of 76 children under 10 years of age, not one has failed to show at least moderate improvement in spite of the difficulties attending parental co-operation.

Severe abdominal pain, presumably of basal origin, may accompany recurrent pulmonary inflammatory attacks especially in children when it may be the only presenting feature. This pain in common with the thoracic type can soon be removed by posturing.

Prophylactic Value: The prophylactic as well as the curative value of the sloping bed needs to be stressed. Brock (1947) has marshalled convincing evidence of the bronchogenic spread of infection from the upper respiratory passages during deep sleep or anaesthesia. Adoption of this posture should do much to hinder such spread at all times.

Facial Oedema: Oedema of the face lasting for several hours after rising may give concern to patients until explained. It may occur to some degree in about 10 per cent of those on the higher elevation but may be soon alleviated by reducing the elevation temporarily. It usually clears up altogether within a few weeks.

Failures: Every effort was made to get replies to questionnaires from those who had not been successful with the treatment or whose success was very limited. However only 12 replied. There were no failures amongst the most seriously affected patients with bronchiectasis and there were only three failures amongst the 31 cases of continuous asthma. Since closing my records one of these three rang me to say she had tried again and was definitely doing much better.

Therefore failures were not governed by the severity of the symptoms or the extent of the disease so much as by other factors, e.g. method and spirit of application, temperament, etc.

SUMMARY

Resolution of attacks of inflammatory disease of the respiratory tract under certain conditions, such as the severity of the infection and/or the lack of resistance of the patient, may be incomplete.

In this way a greater or lesser degree of permanent damage to lungs may be brought about which tends to increase the patient's susceptibility to a recurrence of the attacks with the liability to progressive increase of the damage. As a sequel to such recurrences the pulmonary damage will, in some cases, tend to reach sooner or later, and often sooner, the irreversible states of pulmonary fibrosis and bronchiectasis. Experience of the treatment of such patients by continuous postural drainage over various periods extending up to 18 years has shown that not only will early resolution of such lesions thereby be promoted but the tendency to recurrence or chronicity of the disease can be at least largely and frequently entirely prevented. Such success in prevention may be obtained even in comparatively late stages in the progress of the disease. Achievement of such results, however, will depend essentially on the adequacy of the application of the treatment and may involve in the case of old established disease its continuation for the rest of the patient's life. However, even in such cases, once complete and lasting freedom from all symptoms has been achieved it may prove satisfactory to the patient to omit the treatment provided prompt renewal is made on the slightest warning of return of the symptoms or on the advent of any respiratory infection however slight.

Bronchial asthma, even when not obviously associated with an infective state can be rapidly eliminated if the treatment is applied in the earlier stages, and even in life time sufferers most satisfactory results can still be achieved with every reasonable prospect of their obtaining ultimately complete freedom from all symptoms.

All the available evidence suggests that such relief is brought about by facilitating, by means of the appropriate posture, the outward flow of secretions which otherwise tend to accumulate through physical difficulties hindering their evacuation.

As most of the treatment must always be carried out in the home the informed co-operation of the family physician is an essential pre-requisite towards the achievement of the best results.

RESUMEN

La resolución de los ataques inflamatorios de la enfermedad del tracto respiratorio puede ser incompleta en ciertas condiciones tales como la falta de resistencia del enfermo o la severidad de la infección.

De esta manera puede resultar un grado más o menos considerable de daño permanente en los pulmones que puede acarrear la susceptibilidad del paciente a las recurrencias con la posibilidad de un aumento progresivo del daño. Como secuela de semejantes recurrencias el daño pulmonar, puede en algunos casos, alcanzar o pronto más o menos tarde, más bien rápidamente, un estado irreversible de fibrosis pulmonar y bronquiectasia.

La experiencia con el tratamiento de esos enfermos por medio de la canalización postural por periodos que abarcan hasta 18 años, ha demostrado que no sólo puede conseguirse una temprana resolución de dichas lesiones, sino que la tendencia de la enfermedad a la recurrencia o cronicidad puede por lo menos prevenirse ampliamente. Tales éxitos en la prevención, pueden obtenerse aún en casos tardíos de la enfermedad. Los resultados, señalados, sin embargo, dependen de manera esencial de que la aplicación del tratamiento sea adecuada y puede necesitar en caso de una enfermedad largamente establecida la continuación del tratamiento por el resto de la vida. Sin embargo, aún en aquellos casos se ha logrado poder suspender el tratamiento por haberse logrado en forma satisfactoria para el paciente, una completa y duradera remisión de los síntomas siempre que el enfermo reanude el tratamiento omitido, tan pronto como haya algunos síntomas o aparezca alguna infección respiratoria por pequeña que ésta sea.

El asma alérgico, aunque no esté evidentemente asociado a un estado infeccioso, responderá también con prontitud si el tratamiento es empleado al principio del proceso.

Todas las evidencias están en favor de la opinión de que las secreciones que en otras condiciones difíciles de expeler, pueden por este medio ser expulsadas.

Como el tratamiento debe realizarse en el domicilio del paciente es requisito que cooperen en él, el médico tratante y la familia.

RESUME

La résolution des crises aigues des maladies inflammatoires aigues de l'appareil respiratoire peut être incomplète, quand se réalisent certaines conditions, telles que la sévérité de l'atteinte, compliquée ou non de l'absence de résistance du malade.

Dans ce domaine, on peut invoquer un degré plus ou moins grand de lésions définitives du poumon qui tend à augmenter la prédisposition du malade aux récidives avec possibilité d'un accroissement progressif des lésions. Les récidives auront comme conséquences de hâter l'altération pulmonaire qui atteindra plus ou moins tardivement—et souvent plus tôt—les phases irréversibles de fibrose pulmonaire et de bronchiectasie. L'expérience du traitement de tels malades par drainage de posture continu s'étendant sur différentes périodes, allant jubqu'à 18 ans, a montré que non seulement une résolution précoce de telles lésions pourra être obtenue, mais que la tendance à la récidive ou à la chronicité de l'affection pourra être au moins largement et fréquemment totalement empêchée. Un tel succès dans la prévention peut même être obtenu dans des phases relativement tardives de l'affection; cependant le succès de ces résultats dépendra essentiellement de la façon dont sera conduit le traitement. Il peut nécessiter, quand l'affection évolue depuis longtemps déjà, sa continuation pendant le reste de la vie du malade. Toutefois, même dans de tels cas, lorsqu'on à pu obtenir la disparition complète et durable de tous les symptômes, il peut être souhaitable d'interrompre le traitement. Mais il faudra

le reprendre immédiatement à la moindre suspicion de rechute et à la moindre manifestation d'infection respiratoire, même bénigne.

L'asthme d'origine allergique, même lorsqu'il n'est pas associé d'une façon évidente à un état infectieux, sera également heureusement favorisé par ce traitement, s'il est appliqué dans la phase précoce de la maladie.

Il est démontré que cette action est obtenue en facilitant par une position appropriée, le rejet des sécrétions qui autrement tendrait à s'accumuler par suite des difficultés physiques qui empêchent leur évacuation.

Comme la plus grande partie du traitement doit toujours être poursuivie à domicile, la collaboration éclairée du médecin de famille est un élément essentiel du succès.

REFERENCES

Elwell, L. Bedford: "Continuous Postural Drainage: An Essential Principle in the Treatment of Diseases of the Respiratory Tract," *Medical Journal of Australia*, 1:804, 1949.

Di Rienzo, S.: "Bronchial Dynamism," *Radiology*, 53:168, 1949. Quoted by The 1950 Year Book of Medicine, p. 175.

Hirschfeld, K.: "Some Aspects of Prevention and Treatment of Bronchiectasis," *Medical Journal of Australia*, 1:870, 1951.

Nelson, H. P.: "Postural Drainage of the Lungs," *British Medical Journal*, 2:251, 1934.

Riviere, C.: "Damaged Lungs and Bronchiectasis," *British Medical Journal*, 1:141, 1923.

Nobecourt, P.: "Clinique Medicale des enfants: Affections de l," Appareil Respiratoire Paris Masson et Cie. Quoted by Davidson, loc. cit., p. 247, 1924.

Davidson, Maurice: "A Practical Manual of Diseases of the Chest," pp. 245-246, 1935.

Brock, R. C.: "The Anatomy of the Bronchial Tree," p. 92, loco citato, pp. 8-15.

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Cerebral Air Embolism Complicating Therapeutic Pneumoperitoneum

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The following case study is presented to illustrate the concept that recovery from the invariably disastrous effects of arterial air embolism, accidentally incurred during the therapeutic administration of pneumoperitoneum, may be possible if certain recognized and specific maneuvers are practiced correctly. This particular subject is of extreme importance because since the institution of pneumoperitoneum in the treatment of tuberculosis, 19 fatal accidents have occurred due to embolic complications.[12,13] Three occurred in the Veterans Administration Hospital, Oteen, North Carolina, since 1942, during approximately 150,000 refills given to about 2,400 patients.

The following case represents an embolic accident which fortunately was followed by recovery.

L. J., age 32, known to be suffering from far advanced pulmonary tuberculosis since August 1950, was admitted on October 5, 1950 and two days later was started on chemotherapy consisting of 0.5 gram streptomycin intramuscularly once daily concurrently with four grams of para-aminosalicylic acid, by mouth, three times daily. On November 11, 1950, pneumoperitoneum was induced because, following subsidence of the initial toxic symptoms, it was felt that pulmonary collapse would also be necessary in treatment of the bilaterally extensive exudative and cavitary disease. After one year's continuous combined drug and collapse therapy, an excellent result, with bilateral clearing and cavitary closure, was obtained. Pneumoperitoneum was induced by a standardized procedure using the Zavod apparatus connected by sterile rubber tubing with a glass syringe and number 19 gauge short bevel needle measuring five inches in length. After sterile preparation and infiltration of an area to the left of the umbilicus with one per cent novocaine, 450 cubic centimeters of air were slowly introduced. The intra-abdominal pressure at the end of the injection was equivalent to a positive pressure of two centimeters of water, as measured on the manometer. Refills were repeated at weekly intervals, the amount being gradually increased to 800 cubic centimeters. Novocaine was not used after an adequate air space was obtained. The usual initial positive pressures fluctuated between five and six centimeters of water, the final positive pressures between six and eight centimeters. Fluoroscopy was utilized before each refill to determine the degree of diaphragmatic elevation and to make certain that no complication had developed. These observations demonstrated a fairly stable sub-diaphragmatic air chamber. Until September 20, 1951, at which time the embolic accident occurred, the patient had received 44 refills without incident.

On the day of the accident, the needle was inserted in the usual manner and, after having made certain that a free oscillation of the manometer existed, a reading was taken and the notation made that it approximated a positive pressure of eight centimeters of water. The needle was then quickly withdrawn, after 700 cubic centimeters of air were injected. At the end of the procedure however, a final positive pressure of 18 centimeters of water was noted. He rose slowly from the table, walked a short distance and then suddenly collapsed. An apnoeic phase with severe cyanosis intervened and he became rigid, following generalized tonic

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muscular contractures. The nearest person to the victim turned him on his right side, but this was immediately corrected and he was placed in the left lateral recumbent position. It will be shown later that this position was of virtually no value because stethoscopic auscultation of the heart in this particular instance did not disclose the typical churning mill-wheel murmur diagnostic of the cardiovenous form of air embolism. In quick succession, oxygen by intra-nasal catheter and an injection of 1/150 grain of atropine sulfate were administered. The latter agent was used to relieve respiratory embarrassment because by paralyzing the parasympathetic nerves, it would abolish bronchospasm and therefore dilate the pulmonary bronchi.[8] After several minutes, respiratory movements gradually resumed. As consciousness slowly returned, it was noted that the left arm and leg were completely motionless. He was immediately returned to the operating table and deflation of the pneumoperitoneum was begun. After withdrawal of 1,050 cubic centimeters of air and return of the intraperitoneal pressure to a positive reading of eight centimeters of water, he was able to respond to direct questioning, which now disclosed a disturbance of vision described as a blurring sensation. He had normal blood pressure of 100/70, and frequent subsequent check-ups did not reveal any evidence of the existence of hypotension. Intravenous plasma was later administered on a purely empirical basis. It was given with the hope that it might alleviate the suspected anoxic injury to the brain.[10] The left hemiplegia partially resolved in two hours and the extremities completely returned to normal in four hours. Sedation was used to relieve the severe headache which subsequently developed. This and the blurring vision vanished in 48 hours and to date no permanent disabling residuals have been observed.

Prior to Durant, Long and Oppenheimer's[6] experimental studies on air embolism, the management of such accidents in humans consisted principally of resuscitative measures involving the use of artificial respiration, oxygen, stimulants and the Trendelenburg position. In other words, the treatment in most cases did not differ materially from that customarily employed in ordinary shock. The application of such measures were sometimes but not always successful in the hands of Banyai,[1] Fremmel,[2] Trimble and Wardrip,[3] Warring and Thomas[4] and Rilance and Warring.[5] In 1947, Durant et al published an illuminating treatise on the subject of air embolism in which they distinguished two forms. They described the symptoms and pathogenesis and proposed a method of treatment for each entity. Briefly, they described the pulmonary or venous and the cerebral or arterial form. The site of entry of the air bubble in the former is a systemic vein; in the latter, a pulmonary venous channel. The course of the embolus in the former instance is through the right heart into the pulmonary circulation where it is excreted, of the latter through the left ventricle into a systemic artery, e.g. vertebral or coronary. A large volume of air is necessary to prove fatal in the venous form; a small dose may prove fatal in the arterial form. The cause of death in the former is the formation of an air trap in the right ventricular outflow tract with subsequent cardiac arrest; in the latter the cause is attributed to a coronary occlusion or cerebral damage. The clinical signs are a precordial mill-wheel murmur in the former and, in the latter, the well known signs of a coronary occlusion or of a cerebral accident. In the treatment of the venous form, because it relieves the obstruction by displacing the air trap in the right ventricle, the most favorable position is the left lateral; for the

latter, with one reservation, it is the head down position. The exception to the rule is that the head down position will prevent embolism only if this position is present when the accident occurs; it will not clear the cerebral signs or affect the coronary obstruction if the position is assumed after the accident occurs.

Hollander[11] appears to have been one of the first to successfully apply the recommendations suggested by Durant et al. As he reported, the left lateral position produced immediate recovery in one patient who developed a venous air embolism following a pneumoperitoneum refill. In another, developing a cerebral air embolism under similar circumstances, the head down position assumed before the refill was started, aided recovery. He was less fortunate in the management of a third patient because of unavoidable delay in the application of the correct position. The accident occurred after the patient rose from the table and death followed in a matter of minutes. At autopsy, a perforated vein in the abdominal muscle tissues and frothy blood in the right auricle, ventricle and pulmonary artery were found. The author affirmed that the left lateral position should be maintained until obstruction of the pulmonary conus due to the air embolus is completely relieved even if this requires several hours, and that stimulants and oxygen are of little value unless this precaution is observed.

Some workers[4] believe that air embolism complicating a pneumoperitoneum refill almost always occurs following direct entry of air into a blood vessel. Granted that this is so, it is difficult to conceive how the accidental injection of air into a vein of the abdominal wall could reach the brain without passing through the right heart unless one postulates the existence of anomalous vascular channels. It is known that the inferior epigastric vessels coursing through the abdominal wall communicate at their source with the external iliacs and anastomose above the umbilicus with the superior epigastric branches of the internal mammary which first empty into the subclavian and eventually into the right heart. So, unless there is evidence to support the presence of an interauricular or ventricular septal defect, air cannot reach a cerebral artery if injected into a peripheral venous channel. No clinical evidence of such a defect was uncovered in the case under discussion.

To effectively combat the complications resulting from this type of air embolism, it is necessary not only to be reasonably prompt in the application of the correct maneuver after the accident occurs but also to have a thorough knowledge of the precautions that should be observed in administering therapeutic pneumoperitoneum. Particularly extreme caution should be exercised at the moment of induction because it is at this time that accidents are most prone to occur. As the needle punctures the peritoneum, one should be certain that it reposes in a free space. Any signs of resistance to the flow of air such as is usually indicated by the absence of manometric oscillations, should warn the operator that the needle may be in muscular or connective tissues and that it should be immediately adjusted. If blood appears in the syringe, showing obviously

that some vessel has been punctured, the needle should be immediately withdrawn before air is injected and another site selected. It is good policy, moreover, that, if a certain area of skin has been found to permit facility of introduction of the needle without risk of injuring a blood vessel, the same site be used again if refills are continued. Fluoroscopy should serve primarily as a guide for the determination of the presence or absence of diaphragmatic elevation and should not influence the operator regarding the quantity of air to be injected. The quantity should depend rather on the intraperitoneal pressure and, if it is found that it is unusually high without correspondingly adequate elevation of the diaphragm, serious consideration should be given to abandoning the pneumoperitoneum. A prophylactic measure that enjoys the support of some operators is the use of the Trendelenburg position in all cases before the refill is given. The reason advanced for this is that the resultant flow of the subdiaphragmatic air mass away from the brain is believed to hinder invasion of a damaged blood vessel.[1,12] The para-umbilical injection route is preferred to the infra or intra-costal approach because of the likelihood of puncturing the lung or liver with the latter technique. Such trauma to these organs inevitably produces an embolus if air is introduced with the puncture. Particular attention should be paid to the patient's complaints of dizziness and nausea which, despite the inclination to minimize them, are oftentimes reasonably good indicators of impending disaster. It is advisable also to regulate the flow of air into the peritoneal cavity by injecting, for example, small quantities of 50 cubic centimeters with frequent pressure readings. These precautions, if carefully observed, should eliminate those complications secondary to improper technique but unfortunately will not prevent the rare complication which is due to no fault of the operator. If the accident occurs on the operating table, a meticulous examination will almost consistently give some indication as to the type of procedure that might be of assistance. In the presence of a typical precordial mill-wheel murmur, the left lateral position is the only procedure that will succeed, keeping in mind, however, that it should not be discontinued until the air obstruction is completely relieved and until there is some certainty that the traumatized blood vessel has had a chance to heal. On the other hand, no reliable method of treatment has as yet been devised to manage arterial embolic accidents after the patient has apparently safely completed his pneumoperitoneum refill. Although no claim can be made at present concerning the effectiveness of the decompression technique in these cases, it is nevertheless believed to be worth a trial for the following reason. Where the head down position merely shifts and immobilizes the intraperitoneal air mass, abdominal deflation, on the other hand, helps to remove this potential hazard, thereby offering greater assurance that further embolization will not occur.

SUMMARY

One case with recovery from cerebral air embolism complicating therapeutic pneumoperitoneum is reported. Similar accidents reported in the

literature are briefly discussed and precautions to be observed in administering pneumoperitoneum are reviewed. An additional safeguard represented by abdominal decompression is suggested for managing this complication.

RESUMEN

Se refiere un caso de embolia cerebral gaseosa complicando neumoperitonéo terapéutico, con recuperación. Se han relatado accidentes similares en la literatura los que se discuten así como las precauciones que deben observarse al administrar el neumoperitonéo. Se sugiere una medida adicional consistente en la descompresión abdominal para tratar esta complicación.

RESUME

L'auteur rapporte un cas d'embolie gazeuse cérébrale, compliquant un pneumopéritoine thérapeutique. Il discute rapidement les accidents de cet ordre jusqu'ici rapportés dans la littérature, et énumère les précautions que l'on doit observer lorsqu'on pratique un pneumopéritoine. Il conseille la décompression abdominale en tant que procédé de sécurité supplémentaire.

REFERENCES

1 Banyai, A. L.: "Pneumoperitoneum Treatment," C. V. Mosby Co., 1946.
2 Fremmel, F.: "Phrenicectomy Reinforced by Pneumoperitoneum," *Am. Rev. Tuberc.*, 36:499, 1937.
3 Trimble, H. G. and Wardrip, B. H.: "Pneumoperitoneum in Treatment of Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, 36:111, 1937.
4 Warring, F. C. and Thomas, R. M.: "Spontaneous Air Embolism in Pneumoperitoneum," *Am. Rev. Tuberc.*, 42:682, 1940.
5 Rilance, A. B. and Warring, F. C.: "Pneumoperitoneum Supplementing Phrenic Paralysis," *Am. Rev. Tuberc.*, 44:323, 1944.
6 Durant, T. M., Long, J. and Oppenheimer, M. J.: "Pulmonary (Venous) Air Embolism," *Am. Heart Jour.*, 33:269, 1947.
7 Bailey, W. H.: "Air Embolism in Pneumoperitoneum, Fatal Case," *Am. Rev. Tuberc.*, 57:621, 1948.
8 Sollmann: "Manual of Pharmacology," 7th Ed., pp. 309-320, 1948.
9 Durant, T. M., Oppenheimer, M. J., Webster, M. R. and Long, J.: "Arterial Air Embolism," *Am. Heart Jour.*, 38:481, 1949.
10 Davis, H. A.: "Shock," Grime & Stratton, p. 37, 1949.
11 Hollander, A. G.: "Air Embolism in Pneumoperitoneum," *J.A.M.A.*, 147:568, 1951.
12 Cohen, A. C., Glinsky, G. C., Martin, E. G. and Fetterhoff, K. I.: "Air Embolism," *Ann. Int. Med.*, 35:779, 1951.
13 Stein, H. F.: "Complications of Artificial Pneumoperitoneum," *Am. Rev. Tuberc.*, 64:645, 1951.

Mediastinal Emphysema as a Complication of Pneumoperitoneum Therapy*

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The purpose of this communication is to report four cases of mediastinal emphysema occurring during the course of pneumoperitoneum therapy.

The use of pneumoperitoneum in the treatment of pulmonary tuberculosis is becoming increasingly popular. Drolet surveyed 99 hospitals in 1943[1] and found that pneumoperitoneum was used in less than 1 per cent of their patients and that only 44 of the hospitals utilized this treatment at all. Now, however, pneumoperitoneum is being used on a large scale in many institutions, almost supplanting the use of pneumothorax. Pneumoperitoneum was introduced as a treatment for pulmonary tuberculosis by Vajda[2] in Europe and Banyai[3] and Fremmel[4] in the early 1930's. In spite of the great popularity of this treatment, not much has been published about mediastinal emphysema as a complication. John and Nisson[5] in 1927 mentioned the occurrence of mediastinal emphysema as a complication of pneumoperitoneum, but give no details. Banyai and Jurgens[6] in 1939 reported seven cases of mediastinal emphysema occurring among 42 patients. All were demonstrable on roentgenograms. It is to be noted, however, that their method of inducing pneumoperitoneum (subcostal and intercostal administration) made possible the traumatizing of the diaphragm by the needle. They state thus, "the air elevates the basal parietal pleura, and dissecting it from the upper surface of the diaphragm, reaches the mediastinum." Anderson and Winn[7] reported one case of mediastinal emphysema among 110 patients with pneumoperitoneum. F. Simmonds[8] in 1946 reported four definite and two doubtful cases of mediastinal emphysema among 12,500 pneumoperitoneum refills. These cases were clinically diagnosed without roentgenographic confirmation. All of his patients were seriously ill, although none died. Moyer[9] in 1949 observed one case of mediastinal emphysema among 550 patients receiving pneumoperitoneum. He reduced the amount of air given at refills and continued the treatment cautiously without recurrence of complications. Small and Fremont in 1951[10] reported one case of mediastinal emphysema, proved by roentgenograms and phonocardiographic tracings of a systolic crunch over the apex (Hamman's sign). All symptoms and signs disappeared in two days, but recurred after a refill of 200 cc. of air. Pneumoperitoneum was then discontinued. H. Stein[11] in 1951 discussed the complications of pneumoperitoneum therapy in a comprehensive paper, mentioned the rarity of mediastinal emphysema and presented one proved case.

Case 1: T.L. A 62 year old white male was admitted to Municipal Tuberculosis Sanitarium August 8, 1950, with far advanced pulmonary tuberculosis and positive

*From the Municipal Tuberculosis Sanitarium of Chicago, Illinois.

sputum. He received 1 gm. of dihydrostreptomycin twice weekly, and 12 gm. of PAS daily from September 22, 1950 to April 12, 1951. On April 17, 1951 pneumoperitoneum was started without untoward incident. Thereafter he received refills twice weekly, the manometric readings being within the normal range. Fluoroscopy on April 24, 1951 revealed air beneath the diaphragm with fair elevation of both sides. On April 27, a few minutes after the fifth pneumoperitoneum treatment (600 cc. plus 16 cm. reading) the patient complained of pressure in the neck and occiput. Physical examination revealed crepitation on both sides of the neck, but none over the abdomen or chest. No dyspnea or cyanosis was discernible, nor was there any chest pain. He was kept at bed rest and two hours later the subcutaneous emphysema of the neck increased. He complained of choking and dysphagia. One thousand cc. of air was removed from the abdomen and codeine given for pain. All symptoms and signs gradually disappeared. Roentgenogram revealed air along the left cardiac border (Figure 1). He had a restful night. Mild crepitation of the neck was noted for about one week. Pneumoperitoneum was discontinued.

Case 2: J.R. A 41 year old white male was admitted to this sanatorium on August 7, 1951 with far advanced pulmonary tuberculosis and positive sputum. Dihydrostreptomycin, 1 gm. twice weekly and PAS 12 gms. daily, was started August 23, 1951. Pneumoperitoneum was induced on October 30, 1951 without untoward incident. He was given refills twice weekly with normal manometric readings after each treatment. Fluoroscopy on November 2, 1951 revealed air beneath the diaphragm, with fair elevation of both sides. On November 6, 1951, after the fourth treatment (800 cc. of air plus 10 cm. reading) the patient complained of abdominal distress. Physical examination revealed mild subcutaneous emphysema of the neck. This lasted two days. There were no further complaints. Roentgenogram on November 8, 1951 revealed air along the left cardiac border (Figure 2). On November 9, another refill was attempted (400 cc. of air, plus 6 cm. reading) and he again complained of similar abdominal distress, developing about one hour after the refill. Mild subcutaneous emphysema of the neck appeared

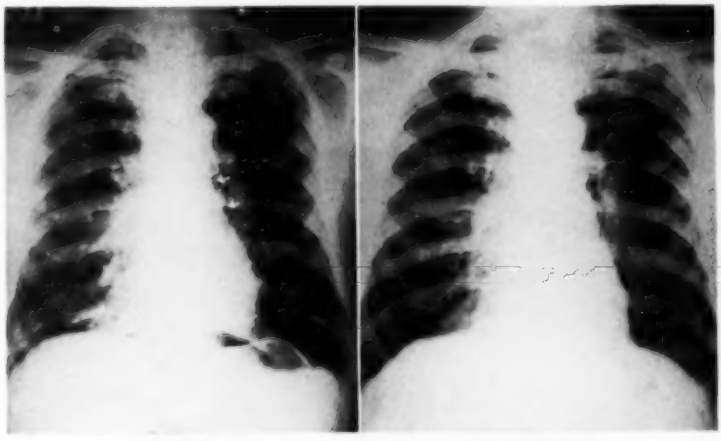

FIGURE 1A FIGURE 1B

Figure 1A, Case 1: T.L. After fifth pneumoperitoneum treatment, April 27, 1951. Subcutaneous emphysema of both sides of the cervical region (mostly on the right). Suspicious radiolucent shadow along the left mid-cardiac border.—*Figure 1B:* After discontinuation of pneumoperitoneum, May 11, 1951. No subcutaneous emphysema of the neck visible. No evidence of mediastinal emphysema.

again. He left the institution against medical advice, and could not be followed further.

Case 3: V.H. A 46 year old white male was admitted on March 19, 1951, with far advanced pulmonary tuberculosis and positive sputum. He previously had right pneumothorax from 1936 to 1946, and left extrapleural pneumothorax from 1940 to 1946. He was given 1 gm. of dihydrostreptomycin daily and 12 gms. of PAS daily, beginning April 8, 1951. The PAS had to be discontinued because of fever and

FIGURE 2A FIGURE 2B

Figure 2A, Case 2: J.R. Admission film on August 7, 1951. Mottled infiltration of left upper lobe with probable cavity.—*Figure 2B:* After fourth pneumoperitoneum treatment, November 8, 1951. Air along the projection of left cardiac border. Streaky radiolucent areas in the cervical subcutaneous tissues.

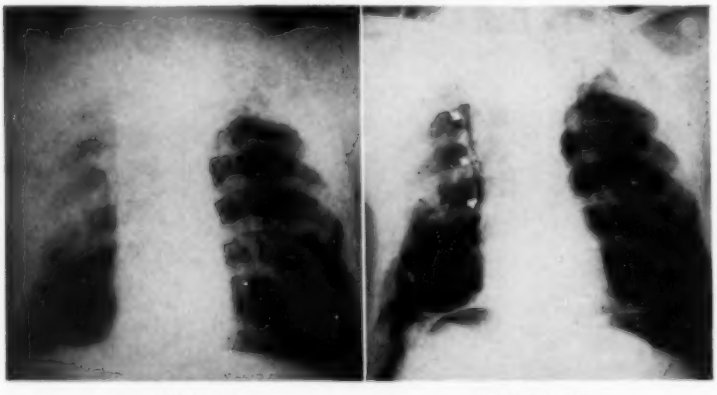

FIGURE 3A FIGURE 3B

Figure 3A, Case 3: V.H. Admission film on March 29, 1951. Homogenous opacification of both apices and infraclavicular regions. Both hemidiaphragms flattened and irregular. Blunting of both costophrenic sinuses.—*Figure 3B:* After mediastinal emphysema 1800 cc. of air was removed from the abdominal cavity, September 4, 1951. Remnants of air beneath the diaphragm. Air along the mediastinum, especially on the right. Subcutaneous emphysema of cervical region.

rash. Pneumoperitoneum was induced on August 28, 1951 without difficulty. He received refills twice weekly with normal manometric readings. On fluoroscopy slight elevation of the diaphragm was observed. On September 3, 1951, i.e. the third day after the third pneumoperitoneum treatment, he suddenly felt a choking sensation after clearing his throat at about 8:30 a. m. His voice became slightly hoarse and he complained of mild dyspnea, with pain in the right side of the neck. Physical examination revealed the presence of moderate subcutaneous emphysema on both sides of the neck, but none over the abdomen or chest. Eighteen hundred cc. of air was removed from the abdominal cavity and he felt much relieved. Pneumoperitoneum was discontinued. Roentgenogram on September 4, 1951, revealed air along the right mediastinal border (Figure 3).

Case 4: P.W. A 35 year old white female was admitted on July 5, 1950, with the diagnosis of pulmonary tuberculosis, far advanced, wioh positive sputum. She was started on 1 gm. of dihydrostreptomycin twice weekly and 12 gms. of PAS daily on August 1, 1950. Pneumoperitoneum was induced on October 2, 1950 without untoward incident. Routine refills were given until December 19, 1950. On December 24, 1950 she was given leave to go home for 24 hours. About 9:00 p. m. the same evening, while at home, she had an attack of retching and emesis after eating a shrimp cocktail, which she blamed for the symptoms. Soon afterwards she developed a choking sensation, was unable to talk, and noted swelling of the face. She was taken from her home to a private hospital where a tracheotomy was suggested, but refused by the patient. She was brought back to us at 3:00 a. m. on December 25, 1950. Physical examination then revealed crepitation of the face, neck and eyelids. No dyspnea was noted. Roentgenograms December 26, 1950 showed marked subcutaneous emphysema of the neck, but not of the thorax. No air was demonstrable in the mediastinum, but a change in the configuration of the heart was noted with a shift to the left (Figure). Pneumoperitoneum was discontinued for the time being. Following a two-stage right thoracoplasty, with subscapular paraffin pack on August 15, 1951 and September 6, 1951, the pneumoperitoneum was reinstituted. She has been receiving routine refills since that time without recurrence of emphysema to date, June 1952.

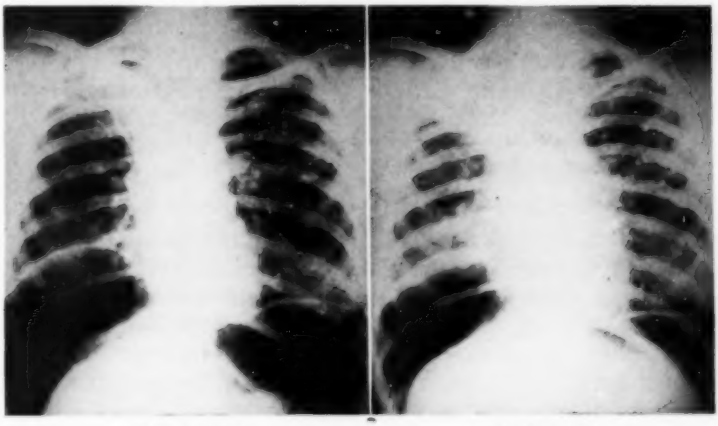

FIGURE 4A FIGURE 4B

Figure 4A, Case 4: P.W. Before the incident, December 12, 1950. Pneumoperitoneum with fair elevation of both hemidiaphragms.—*Figure 4B:* Two days later, December 26, 1950. Less air beneath the diaphragm. Evident subcutaneous emphysema of neck tissues, no discernible air in the soft tissues of the thoracic wall. Heart configuration changed when compared with previous film; slightly shifted to the left.

Pathogenesis

Opinions differ regarding the route taken by the air which reaches the mediastinum from the peritoneal cavity. If the traumatic possibilities (such cases as may follow intercostal needling) are excluded, there are three groups of opinions: (1) Banyai,[6] Simmonds,[8] and Moyer[9] believe the air escapes from the peritoneal cavity through a weak portion of the peritoneum into the retroperitoneal space, thence proceeding along the large vessels to the natural hiatuses of the diaphragm and through them into the mediastinum. (2) Some authors (e.g. Newlyn Smith[12]) believe that air may find its way through small congenital defects in the diaphragm. Smith published a report of a case which showed upon autopsy a few small, apparently congenital openings in the diaphragm. Other authors, e.g. Sita Lumsden[13] mentioned an open pleuro-peritoneal canal on the right side. If this is fully open the induction of pneumoperitoneum may be immediately followed by mediastinal emphysema and/or pneumothorax. If there is loose adherence, i.e. only potential communication between the two cavities, the complication occurred only with suddenly increased intra-abdominal pressure. (This is an analogy to an open inguinal ring in which a scrotal pneumocele may occur after induction of pneumoperitoneum). (3) Accidental rupture of the diaphragm in the course of pneumoperitoneum: Fatal cases usually occur only when accompanied by tension pneumothorax, complicating the pneumopertioneum therapy. Yanitelli and co-workers[14] published such a case in which at autopsy a 2 mm. round opening was found on the peritoneal surface of the diaphragm leading into a large bleb on the pleural surface of the diaphragm. Mitchell[15] mentioned also a diaphragmatic rupture complicating pneumoperitoneum. Spencer and Yuill[16] published a case report in which rupture of the diaphragm complicated pneumoperitoneum, the site of leakage being proved by thoracoscopy. The above cases mentioned by Smith, Yanitelli, Mitchell, and Spencer all had pneumothoraces complicating pneumoperitoneum and are mentioned here only because of the authors opinions regarding the route of air from the abdominal cavity into the chest. This route could theoretically be the same as that which produces mediastinal emphysema.

The Symptoms and Clinical Course of Mediastinal Emphysema

The onset of symptoms may start a few minutes, a few hours, or a few days after air is introduced into the peritoneal space. This fact is frequently of value in the differential diagnosis from air embolism which usually occurs *during* the introduction of air. The occurrence of convulsions, characteristic of air embolism, have never been reported in mediastinal emphysema. Mediastinal emphysema frequently occurs after a sudden increase of intra-abdominal pressure due to coughing, emesis, bowel movement, or change in position.

The most common symptoms are substernal distress, throat pain, choking sensations, dysphagia, hoarseness or aphonia, and more or less dyspnea. Examination may reveal palpable subcutaneous emphysema over the abdomen or chest. Hamman[17] described the crunching sound which can be

heard over the precordium with each heart beat. (See cases reported by Small and Fremont[10]). Roentgenograms reveal the presence of a thin layer of air following the left or right heart border and may also show the air in the subcutaneous tissues of the neck.

After mediastinal emphysema has occurred, air may further distribute itself (1) to the neck, producing subcutaneous emphysema in this region. Simmonds[8] called this route a safety valve. (2) To the pleural space, producing pneumothorax (usually on the right). (3) To the lung tissue, resulting in interstitial emphysema of the lung stroma (this happens rarely and is very dangerous).

Treatment

In mild cases observation and bed rest may be all that is necessary. In moderate or severe cases it is probably wise to remove air from the abdominal cavity, or at least to decrease the intra-abdominal pressure. Sedatives may be helpful to prevent anxiety and restlessness. Inhalation of oxygen may be necessary if dyspnea and cyanosis occur. If pressure in the mediastinum is severe, the introduction of a canula above the manubrium and aspiration of air by means of a pneumothorax apparatus may be performed. If pneumothorax has occurred, air may also be removed from the pleural cavity in the usual manner.

After this complication occurs pneumoperitoneum usually is discontinued; however, Banyai[6] advised that in mild cases the pneumoperitoneum can be continued with caution. Moyer[9] and Stein[11] continued refills in their cases without recurrence of the complication.

SUMMARY

Four cases of mediastinal emphysema are reported occurring as a complication of pneumoperitoneum for pulmonary tuberculosis. All were confirmed by roentgenograms. A brief survey of the medical literature regarding this complication is given. The symptoms, signs, clinical course, pathogenesis, and therapy are discussed.

RESUMEN

Se relatan cuatro casos de enfisema mediastinal como una complicación del neumoperitoneo en tuberculosis pulmonar. Todos fueron confirmados por roentgenogramas. Se presenta un breve resumen de la literatura médica en relación con esta complicación. Se discuten los síntomas signos, evolución clínica y tratamiento.

RESUME

L'auteur rapporte quatre cas d'emphysème médiastinal venant compliquer des pneumopéritoines institués pour tuberculose pulmonaire. Tous furent confirmés par radiographie. L'auteur fait une revue rapide de la littérature médicale concernant cette complication. Il met en discussion les symptômes, l'évolution, la pathogénie et le traitement.

REFERENCES

1 Drolet, G. J.: "Collapse Therapy," *Am. Rev. Tuberc.*, 47:184, 1943.
2 Vajda, L.: "Can One Employ Pneumoperitoneum in the Collapse Therapy of Pulmonary Tuberculosis," *Zeitschrift Fuer Tuberc.*, 67:371, 1933.
3 Banyai, A. L.: "Therapeutic Pneumoperitoneum—A Review of 100 Cases," *Am. Rev. Tuberc.*, 29:603, 1934.
4 Fremmel, F.: "Phrenicotomy Reinforced by Pneumoperitoneum," *Am. Rev. Tuberc.*, 36:488, 1937.
5 John, W. and Nissen, R.: "Pathologie und Klinik des Mediastinal Emphysema," *Deutsche Zeitschrift Fuer Chirurgie*, 206:221, 1927.
6 Banyai, A. L. and Jurgens, G. H.: "Mediastinal Emphysema as a Complication of Artificial Pneumoperitoneum," *Jour. Thor. Surg.*, 8:329, 1939.
7 Anderson, N. L. and Winn, N. D.: "Pneumoperitoneum and Diaphragm Paralysis," *Am. Rev. Tuberc.*, 52:380, 1945.
8 Simmonds, F. A. H.: "Air Embolism and Pneumo-mediastinum in Artificial Pneumoperitoneum," *Lancet*, 1:530, 1946.
9 Moyer, R. E.: "Pneumoperitoneum and Phreniclasia in the Treatment of Pulmonary Tuberculosis," *Dis. of Chest*, 15:43, 1949.
10 Small, M. J. and Fremont, R. E.: "Mediastinal Emphysema Complicating Induction of Pneumoperitoneum," *Am. Rev. Tuberc.*, 63:591, 1951.
11 Stein, H. F.: "Complications of Pneumoperitoneum," *Am. Rev. Tuberc.*, 64:645, 1951.
12 Smith, Newlyn C. letter: "Induced Pneumoperitoneum: A Fatal Case," *Brit. Med. Jour.*, 2:404, 1943.
13 Sita Lumsden, E. G.: "Spontaneous Pneumothorax Complicating Artificial Pneumoperitoneum," *Thorax*, 4:147, 1949.
14 Yanitelli, S. A., Woodruff, C. E., Mueller, E. E. and Howard, W. L.: "Fatal Tension-pneumothorax Resulting from Diaphragmatic Rupture in a Patient Receiving Pneumoperitoneum," *Am. Rev. Tuberc.*, 60:794, 1949.
15 Mitchell, Roger S., Hiatt, J. S. Jr., McCain, P. P., Easom, H. F. and Thomas, C. D.: "Pneumoperitoneum in the Treatment of Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, 55:306, 1947.
16 Spencer, J. and Yuill, K. C.: "Spontaneous Pneumothorax Resulting from Pneumoperitoneum Therapy," *Brit. Jour. Tuberc.*, 46:30, 1952.
17 Hamman, L.: "Spontaneous Mediastinal Emphysema," *Bull. Johns Hopkins Hosp.*, 64:1, 1939.

Tuberculosis of the Tongue: Report of a Case*

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Tuberculosis of the tongue is one of the less common lesions caused by the tubercle bacillus. Morgagni[1] in 1761 first described a case, and in the 191 years since then only about 500 additional cases have been reported.[2] Since the tongue of every patient with active pulmonary tuberculosis is exposed to positive sputum, the relative infrequnecy of tuberculosis of the tongue must be explained. It is probably due to a combination of reasons—the thickness of the mucous membrane, the resistance of striated muscle to tuberculosis, the cleansing action of saliva, and the well-nigh perpetual motion of the tongue.[3]

In theory tuberculosis of the tongue may be either primary or secondary. However, all reported cases occur late in the course of pulmonary tuberculosis, to which they are secondary.

Tubercle bacilli may reach the tongue by extension (that is, through the sputum or by direct extension from a nearby structure). Alternatively the bacilli may gain access to the tongue by way of the blood-stream, or by lymphatic extension. Katz[4] studied a group of cases and believed that in 89 per cent the tongue is infected through the sputum; others hold that hematogenous dissemination plays a greater role.

Tuberculosis may involve any surface of the tongue, the edge and tip being the commonest sites. It may manifest itself as an ulcer—by far the commonest form—a fissure, a granuloma, a tuberculoma, or a diffuse glossitis.

The lesion develops slowly and is painless at first; but after ulceration occurs pain is a prominent feature. If there is no specific treatment, or if treatment fails, pain is likely to become constant, severe, and progressive.

The prognosis and treatment have changed completely since the coming of chemotherapy. In 1945 there was no adequate treatment. If the underlying pulmonary disease could be controlled by rest and collapse therapy, and if the sputum could be made negative, the lesion of the tongue might heal; otherwise it usually progressed. Local treatment was mainly palliative, consisting of ultraviolet radiation, roentgen radiation, cauterization, excision, local anesthesia, and injection of the lingual nerves. The prognosis was poor: 65 per cent were dead within six months after the first symptom and 93 per cent within two years.[4] Since the use of chemotherapeutic agents this forbidding course of events has been reversed. Streptomycin has helped heal tuberculous lesions of the tongue, the prognosis has become fairly good, and pain is slight and easy to control.[5-7]

Streptomycin is not always successful, however. It is desirable to have another effective drug which might be used along with streptomycin or

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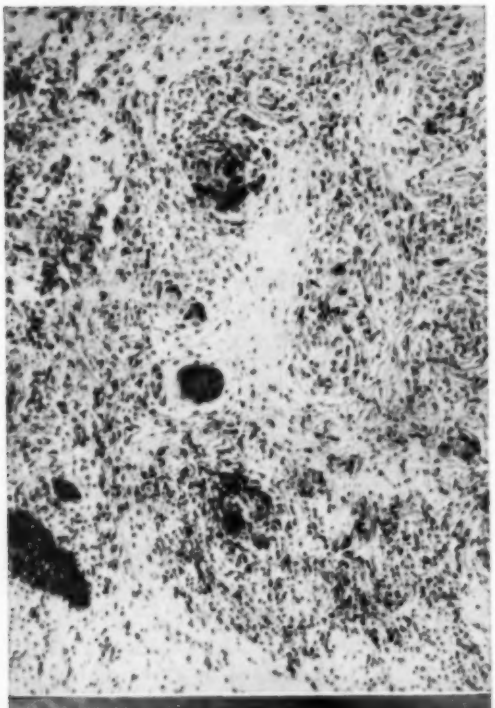

FIGURE 2: x 150

FIGURE 1: April 15, 1952

which might be used in its place when streptomycin is unsuccessful. Isoniazid is such a drug.[8]

Report of Case

M.A., a white man, 28 years of age, was admitted to the Veterans Administration Hospital, Butler, Pennsylvania, on April 10, 1952, for the treatment of far-advanced active pulmonary tuberculosis. For almost a year prior to admission he had been aware of an ulcerative lesion on the dorsum of his tongue. At first a diagnosis of vitamin deficiency had been made, but treatment with vitamins did not produce any benefit. Sixty days prior to admission a course of chemotherapy was started, consisting of streptomycin 1 gram daily. The pulmonary lesion improved and the sputum became negative for tubercle bacilli, but the ulcer did not improve.

Examination of the tongue on admission showed on the dorsal surface, in the midline, a shallow ulcer with an irregular outline, 5 cm. x 1 cm. The remainder of the tongue was coated and whitish in color, and the ulcer, being reddish, stood out in bold contrast. The lesion was hard and had considerable induration at the periphery. The edges were undermined and ragged, and in two places there was a deep fissure; the combined length of the two fissures was about 4 cm. The ulcer was covered by a dirty gray exudate. There were several small but palpable and slightly tender nodes on both sides of the neck. The ulcer was not painful or tender, but the passage of hot or highly seasoned food over it caused some pain.

Biopsy of the involved area was made on May 1, 1952, and the pathological diagnosis was tuberculosis. The microscopic report stated: "Biopsy reveals a granulomatous inflammatory process distributed through the supportive tissue. The overlying epithelium is altered where the nodules involve basal layers of cells; in one area a chronic ulcer has resulted . The granulomatous nodules are composed of epithelioid cells and Langhans giant cells. The characteristic lymphocytic infiltration is largely absent." Acid fast bacilli were demonstrated in the tissues.

On April 22, 1952, chemotherapy was restarted, with streptomycin 2 grams once weekly and para-aminosalicylic acid 12 grams daily. This was continued until June 24, 1952, so that in all a total of 78 grams of streptomycin and 720 grams of para-aminosalicylic acid had been administered over a period of four months. The ulcer did not benefit from this treatment. In fact there was a series of small hemorrhages from the tongue, the largest of which resulted in the loss of about 4 cc. of blood.

Since an adequate trial of streptomycin had failed to cause any perceptible benefit, isoniazid was substituted beginning June 25, 1952. The dosage was 300 mgm. daily, or 5 mgm. per kg. body weight. There were no more hemorrhages. Pain, never prominent, disappeared completely within a week. The ragged edges of the ulcer smoothed out, the dirty exudate covering the ulcer disappeared, and in less than a month the entire ulcerated and fissured area was covered with healthy pink epithelium.

As far as the underlying pulmonary lesion is concerned, there has been no improvement. Serial x-ray films show no change, appetite is only fair, and weight has remained stationary.

SUMMARY

1) A case is reported of an extensive ulcer and fissure on the dorsum of the tongue, proved to be tuberculous by pathological examination of a biopsy specimen and demonstration of acid-fast bacilli in the tissue.

2) This lesion failed to respond to treatment with streptomycin and PAS, but healed in less than a month when treated with isoniazid.

3) The underlying pulmonary disease was not benefited by isoniazid, nor was there any gain in weight or other symptomatic improvement.

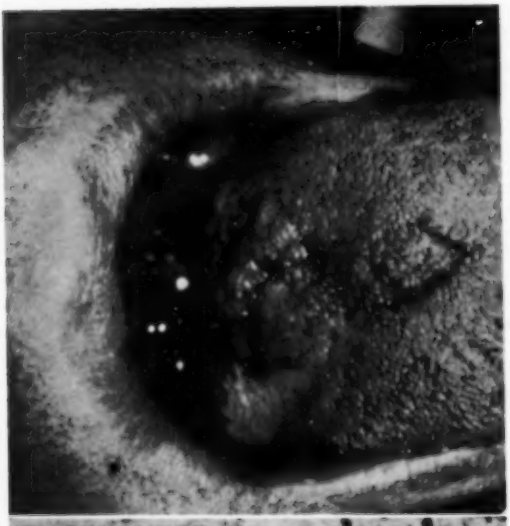

FIGURE 4: July 25, 1952

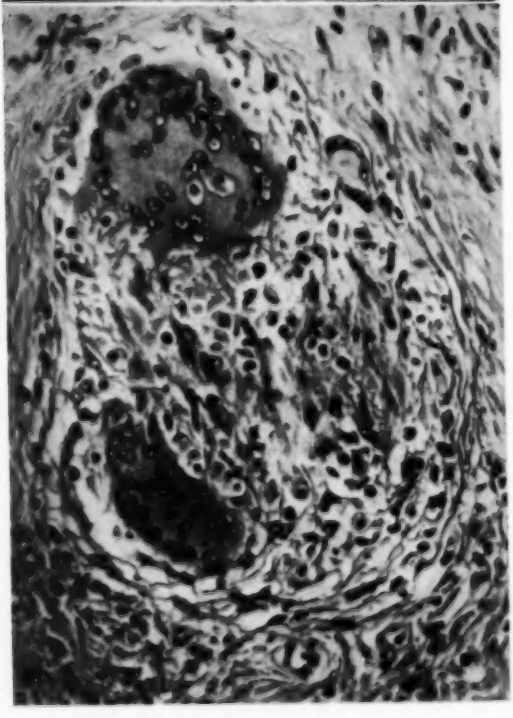

FIGURE 3: x 500

4) Localized lesions such as tuberculosis of the tongue may be improved or cured even while more significant underlying disease is not benefited.

5) Chemotherapy has completely altered the prognosis and treatment of tuberculosis of the tongue.

RESUMEN

1) Se presenta un caso de tuberculosis de la lengua, con gran ulceración y fisura cuya etiología se demostró por la biopsia y hallazgo de bacilos de la tuberculosis en los tejidos.

2) Esta lesión no respondió al tratamiento con estreptomicina y PAS, pero curó en menos de un mes con isoniacida.

3) La enfermedad pulmonar concomitante no fué beneficiada por la isoniacida ni hubo aumento de peso u otro síntoma de mejoría.

4) Las lesiones localizadas tales como la tuberculosis de la lengua, pueden mejorarse o curar aún cuando no haya beneficio apreciable en la enfermedad concomitante.

5) La quimioterapia ha cambiado completamente el pronóstico de la tuberculosis de la lengua.

RESUME

1) Les auteurs rapportent un cas d'ulcère extensif et de fissure du dos de la langue, qui se révéla être tuberculeux après examen anatomopathologique d'une coupe de biopsie et constalation de la présence de bacilles alcoolo-résistants dans les tissus.

2) Cette lésion répondit à peine au traitement par la streptomycine-P.A.S., mais céda en moins d'un mois au traitement par l'isoniazide.

3) L'affection pulmonaire sous-jacente ne fut pas améliorée par l'isoniazide, il n'y eut pas non plus de gain de poids ou d'autre amélioration symptomatique.

4) Des lésions localisées tel les que la tuberculose de la langue peuvent être améliorées ou guéries même si une affection sous-jacente plus importante n'est pas améliorée.

5) La chimiothérapie à complètement changé le pronostic et le traitement de la tuberculose de la langue.

REFERENCES

1 Morgagni, G. B.: "De sedibus et causis morborum per anatomen indigatis," 1761, lib. 5,444.

2 Schneider, Paul: "Streptomycin Therapy of Lingual Tuberculous Ulcer," *Quart. Bull. Sea View Hosp.*, 11:21, 1949.

3 Titche, L. L.: "Tuberculosis of the Tongue," *Am. Rev. Tuberc.*, 52:342, 1945.

4 Katz, H. L.: "Tuberculosis of the Tongue," *Quart. Bull. Sea View Hosp.*, 6:239, 1941.

5 Shamaskin, A.: "Tuberculous Ulcers of the Tongue—Three Cases," *Am. Rev. Tuberc.*, 56:419, 1947.

6 Wolfer, H., Hirshleifer, I. and Shapiro, R.: "Treatment of Tuberculous Ulcer of the Tongue with Streptomycin," *J.A.M.A.*, 136:249, 1948.

7 Oppenhein, H., Livingston, C. S., Nixon, J. W. and Miller, C. D.: "Streptomycin Therapy in Oral Tuberculosis," *Arch. Otolaryngology*, 52:910, 1950.

8 Mamlok, E., Robitzek, E. H. and Selikoff, I. J.: "Tuberculosis of the Tongue: Treatment with Hydrazine Derivatives of Isonicotinic Acid," *Quart. Bull. Sea View Hosp.*, 13:125, 1952.

Undergraduate Teaching of Pulmonary Tuberculosis

EDWARD W. HAYES, M.D., F.C.C.P.*
Monrovia, California

Diseases of the chest was left more or less by the wayside in the development of the programs that have been carried out in our medical schools. This is understandable since well within the professional life of many of us, diseases of the chest consisted almost entirely of tuberculosis and the common pneumonias and their complications. Also in those earlier years there was relatively little known to teach about the diagnosis, control and treatment of even these few diseases.

In the more recent years—that is, within the past two or three decades, as a result of improvement in diagnostic facilities and therapeutic measures, there has been a marked increase in the scope and in the importance of diseases of the chest in medical practice and in medical teaching. Notwithstanding the increase in the magnitude of this branch of medical practice, pulmonary tuberculosis still remains the outstanding public health, economic and medical problem in this category if not in the whole field of medicine. In the attempt to stress the present position of tuberculosis the slogan for the 1953 meeting of the California Tuberculosis and Health Association was "Tuberculosis Still Unconquered."

Only recently has it been recognized that the most important and at the same time the most neglected factor in the fight against pulmonary tuberculosis has been the inadequacy with which medical schools have taught this subject. It was with this recognition that the American College of Chest Physicians adopted as one of its original and primary objectives the determination to bring to the attention of medical schools the importance of pulmonary tuberculosis and to assist them in every way possible in the more effective teaching of diseases of the chest.

It is a source of satisfaction to know that other organizations have now taken up this same objective. It is the hope that in the near future all medical schools will be teaching this subject on a basis that is commensurate with its importance.

Experience has demonstrated that in order to teach diseases of the chest, and especially pulmonary tuberculosis efficiently, certain factors are essential. They are:

First: That suitable teaching material be available;

Second: That this material be presented to the students in a manner that will enable them to acquire a working knowledge of the diagnosis, control and treatment of these particular diseases;

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This is the twelfth and last of a series of articles prepared under the sponsorship of the Council on Undergraduate Medical Education of the American College of Chest Physicians.

Third: That this subject must be taught by teachers who not only have an inherent ability to teach but who also have special interest in this field and who by training and experience are qualified to teach diseases of the chest.

In a long drawn out disease such as pulmonary tuberculosis, characterized by unforeseen and unpredictable changes, it is only possible for the student to gain a practical working understanding and a lasting impression of the various phases of the disease when he has an opportunity to observe and to study the disease through its protracted course.

It is the rare university teaching hospital that today has any facilities for teaching diseases of the chest, particularly tuberculosis, with the result that a large proportion of medical students still graduate without having had any opportunity for bedside observation or study or follow up care of tuberculous patients under conditions where it is possible to carry out the basic principles of treating this disease. While patients with pulmonary tuberculosis may be available in sufficient numbers to medical schools they may not be suitable teaching material. The presentation to students of patients who are domiciled in the wards of general hospitals or under other conditions where it is not possible to carry out the organized and systematic basic principles of treating pulmonary tuberculosis only leaves the students bewildered.

Insistent claims are made that diseases of the chest can and should be taught as an integral part of internal medicine. Attempts to teach diseases of the chest as an intrinsic part of the course in internal medicine have been characterized by failure. When the attempt is made to teach tuberculosis in this way, all too frequently students, during their entire course, see only the few isolated tuberculous patients who find their way into the wards of general hospitals. It is contended that if diseases of the chest is taught as an intrinsic part of the course in internal medicine students have a better opportunity to incorporate the knowledge they acquire about these diseases with what they learn about the other phases of internal medicine. This in theory is good. However, the end results are that the physician trained in this manner in practice when confronted with these diseases, particularly pulmonary tuberculosis, leaves the patient confused and frustrated.

Again when the course in diseases of the chest is offered as a direct component of the course in internal medicine it is as a rule, taught by a teacher whose major interests and his training and experience do not include diseases of the chest, especially pulmonary tuberculosis.

Efforts that will accomplish the needed improvement in the methods of teaching diseases of the chest must be sufficiently comprehensive to afford an opportunity for improvement to all our medical schools. A number of schools are so located geographically that it is not possible for them to provide a sufficient number of patients to fulfill the requirements for teaching material.

At the present time serious effort is being made by the Council on Undergraduate Medical Education of the American College of Chest Phys-

icians to collect from all possible sources x-ray pictures and slides and films. From this general collection it is proposed to make a very careful selection of x-ray pictures and slides and films representing the various diseases of the chest that can be reproduced and supplied to those schools who need and desire such supplementary material. A number of schools have stated that they have material which they could contribute to such a collection and many schools indicated that they would desire to have the material as finally prepared.

It is felt that by the use of x-ray pictures and slides and perhaps to a less extent short films, the basic factors in the diagnosis, prevention and treatment of diseases of the chest can be effectively presented to the medical student. A number of teachers are now adequately teaching diseases of the chest primarily through the use of this type of material which they have collected, for the most part, from their own practice. It is always imperative that, at least, a few patients with the more common diseases of the chest can be provided as teaching material—first, to enable the physician to acquaint the students with the diagnostic and therapeutic approach to the patient, the patient's response to this approach, and how this response should be met. Second, to enable the physician to demonstrate to the students what is most important—the technique of treating the patient as an individual.

The basic aim in undergraduate teaching of diseases of the chest should be to afford medical students an opportunity to obtain an understanding and a practical working knowledge of these diseases so that as physicians they will be "lung conscious" and by their advice and guidance of patients they will be able to supply the missing link that will close that very dangerous and often tragic gap between the general practitioner and the specialist.

Annual Meeting, Board of Regents

AMERICAN COLLEGE OF CHEST PHYSICIANS

Fairmont Hotel, San Francisco, June 17-20, 1954

The annual meeting of the Board of Regents of the College was held on Thursday, June 17, 1954 at the Fairmont Hotel, San Francisco, California and the closing meeting of the Board was held on Sunday, June 20. The following members, council and committee chairmen, and guests were present:

Donald R. McKay, Buffalo, New York, Chairman, presiding
Donato G. Alarcon, Mexico City, Mexico
R. S. Anderson, Erie, Pennsylvania
Albert H. Andrews Jr., Chicago, Illinois
Carl C. Aven, Atlanta, Georgia
Andrew L. Banyai, Milwaukee, Wisconsin
Alvan L. Barach, New York, New York
Otto L. Bettag, Chicago, Illinois
John F. Briggs, St. Paul, Minnesota
John S. Chapman, Dallas, Texas
Seymour M. Farber, San Francisco, California
Carl H. Gellenthien, Valmora, New Mexico
Alfred Goldman, St. Louis, Missouri
Burgess L. Gordon, Philadelphia, Pennsylvania
Alvis E. Greer, Houston, Texas
Edward W. Hayes, Monrovia, California
Paul H. Holinger, Chicago, Illinois
Willard B. Howes, Detroit, Michigan
William A. Hudson, Detroit, Michigan
Hollis E. Johnson, Nashville, Tennessee
Edgar Mayer, New York, New York
Herman J. Moersch, Rochester, Minnesota
Jay Arthur Myers, Minneapolis, Minnesota
James M. Odell, The Dalles, Oregon
Richard H. Overholt, Brookline, Massachusetts
J. Winthrop Peabody, Washington, D. C.
Charles K. Petter, Waukegan, Illinois
Joseph C. Placak, Cleveland, Ohio
James H. Stygall, Indianapolis, Indiana
David H. Waterman, Knoxville, Tennessee
Irving Willner, Newark, New Jersey
Murray Kornfeld, Chicago, Illinois, Executive Director
Harriet L. Kruse, Chicago, Illinois, Executive Assistant
S. N. Turiel, Chicago, Illinois, Executive Assistant

Reports were presented by the following councils and committees, which will be published in subsequent issues of *Diseases of the Chest:*

Council on Undergraduate Medical Education
Council on Postgraduate Medical Education
Council on Hospitals
Council on Research
Committee on Occupational Diseases of the Chest
Committee on Chest X-ray
Committee on Audiovisual Aids
Committee on Indian Affairs

Dr. Myers, Chairman of the Editorial Board for *Diseases of the Chest*, presented the following report:

> The annual report indicates that more manuscripts are being published yearly due to the efforts of the Editorial Board in reducing the length of the manuscripts, together with the use of fewer tables and illustrations, wherever possible. It is recommended that those responsible for the editing of manuscripts make every effort to reduce the number of references to a practical and reasonable limit.
>
> The Chairman wishes to recommend to the Board of Regents that Dr. Richard H. Overholt and Dr. Milton W. Anderson, whose terms expire this year, be re-elected to the Editorial Board.
>
> It is recommended that the same number of associate editors be maintained and that there be no change for the ensuing year.
>
> The Editorial Board further recommends that Dr. Theodore Noehren, Vice Chairman of the Council on Undergraduate Medical Education, continue with his series of articles on the modern concepts of the teaching of diseases of the chest for an additional year.

Upon motion made and duly seconded, the report of the Editorial Board was unanimously approved. Dr. Stygall moved that the Board of Regents extend its appreciation to Dr. Myers for his excellent work. Dr. Moersch seconded the motion and it was unanimously adopted.

The Committee on Cardiovascular Disease recommended that short, timely articles devoted to cardiovascular diseases be published in each issue of the College journal, *Diseases of the Chest*. The Board of Regents approved the recommendation and Dr. Arthur M. Master, New York City, was appointed to prepare these articles.

The following report of the Committee on Membership was read:

> Since the last Annual Meeting, 548 new members were admitted into the College and 77 Associate Fellows were advanced to Fellowship. The present membership of the College is 4,787 and our members reside in 80 countries or territories.
>
> These members are classified as 13 Honorary Fellows, 3,323 Fellows, 318 Associate Fellows and 1,133 Associate Members.
>
> In addition to the above members, as of May 31, 1954, we had a total of 89 applications pending approval by the Board of Regents. Of this total, 53 are for Fellowship, 17 for Associate Fellowship, 10 for Associate Membership and 9 for advancement to Fellowship. These applications will be reviewed by the Board of Regents at the Semi-annual Meeting of the College, to be held in Miami, Florida, November 28-29, 1954.
>
> The eighth issue of the College Directory listed 4,016 members in 69 countries and territories. There are approximately 1,000 new members whose names are not listed in this directory. Information for the ninth issue of the Directory is now being compiled and it is hoped that the new edition will be available early in 1955.

Dr. Banyai reported that the new book *Nontuberculous Diseases of the Chest*, sponsored by the College, is now off the press and will be available in August of 1954. Announcement was also made of a proposed book on *Roentgenology of the Chest* to be published under the sponsorship of the College. Dr. Coleman B. Rabin, New York City, will serve as chairman of the editorial committee for this new book.

Dr. Edgar Mayer, President of the Common Cold Foundation, reported on the activities of this foundation. He stated that the Foundation has opened offices in New York City and that an intensive campaign for funds is being planned.

Dr. Petter, Treasurer, presented the following report:

STATEMENT OF INCOME AND EXPENSES FOR THE YEAR ENDED DECEMBER 31, 1953

INCOME:		
Annual Dues		$77,351.11
Fellowship Fees		26,980.00
Sales—		
Advertising	$35,734.98	
Subscriptions	19,874.85	
Exhibit Space	1,331.28	
Directory—Net	221.17	
College Services—Net	5,398.15	
	$62,560.43	
Less—Discount Allowed	5,782.12	56,778.31
Interest Received on U. S. Savings Bonds		832.50
Total Income		$161,941.92
EXPENSES:		
Salaries	$43,712.67	
Printing Journal	39,771.47	
Annual Meeting	4,947.47	
International Meeting	4,294.28	
Building Account	4,374.58	
Printing and Engraving	3,856.83	
Handling and Posting Journal	5,170.29	
Postage and Shipping	3,529.65	
Officers' and Committee Expense	3,851.96	
Telephone and Telegraph	1,959.14	
Office Expense	2,120.37	
Traveling—Executive Director	1,958.77	
Semi-Annual Meeting—Board of Regents	815.27	
Public Relations Expense	1,453.95	
Editor of Journal	1,800.00	
Library Expense	466.78	
Membership Certificates	238.21	
Payroll Taxes	416.79	
Employment Agency Fees	387.50	
President's Secretarial Expense	300.00	
Prize Essay Award	300.00	
Audit	250.00	
Contribution to World Medical Assn.	500.00	
College Medal	100.00	
Contribution to Natl. Society for Medical Research	25.00	
Depreciation—Furniture and Fixtures	983.40	
Total Expenses		127,584.38
Net Income		$ 34,357.54

The following resolutions were presented and unanimously approved by the Board of Regents:

BE IT RESOLVED, That the American College of Chest Physicians adopt Regulation No. 9 of the Scientific Exhibit of the American Medical Association, as follows: "ADVERTISING: No advertising matter of any description may be distributed nor any material shown which in any way serves for commercial propaganda. No sales may be made, nor orders taken (for even non-profit bearing enterprises)."

BE IT FURTHER RESOLVED, That the chairman of the Committee on Scientific Program of the American College of Chest Physicians inform each participant in the scientific program and scientific exhibits of the College to this effect.

WHEREAS, It has been known for many years that there are at least two million diabetics under active treatment in the United States and in addition, two million other people who may have evidence of mild disease and,

WHEREAS, It is known that the incidence of tuberculosis is higher in diabetics than in the normal population,

THEREFORE BE IT RESOLVED, That the American College of Chest Physicians go on record as recommending to medical specialists that known diabetics have a chest x-ray every six months instead of yearly x-rays as recommended for the general population so as to detect tuberculosis in the earliest stage possible when treatment of both conditions, tuberculosis and diabetes, is most effective and successful.

The above resolution was introduced by Dr. Edward A. Piszczek, Forest Park, Illinois. Upon motion by Dr. Banyai and duly seconded, this resolution was amended to include primary bronchogenic carcinoma for frequent chest x-ray study to detect tuberculosis.

The following were elected by the Board of Regents:

Committee on Nominations: Jay Arthur Myers, Minneapolis, Minnesota.
Executive Council: Seymour M. Farber, San Francisco, California.
Chairman, Board of Regents: Donald R. McKay, Buffalo, New York.

Announcements:

Registration at the 20th Annual Meeting of the College was 1,150.

The Interim Session and semi-annual meeting of the Board of Regents would be held at the Delano Hotel, Miami Beach, Florida, November 28-29, 1954.

The 21st Annual Meeting of the College would be held in Atlantic City, New Jersey, June 2 through 5, 1955.

9th Annual Postgraduate Course in Diseases of the Chest, sponsored by the Council on Postgraduate Medical Education of the College, Chicago, Illinois, October 18-22, 1954.

Postgraduate course in diseases of the chest, to be sponsored by the Cleveland Society for Diseases of the Chest and the American College of Chest Physicians, will be held at the Frank E. Bunts Educational Institute, affiliated with the Cleveland Clinic Foundation, Cleveland, Ohio, October 27 and 28, 1954.

7th Annual Postgraduate Course in Diseases of the Chest, sponsored by the Council on Postgraduate Medical Education of the College, New York City, November 8-12, 1954.

1954 Prize Essay Contest

At the Annual Presidents' Banquet of the College held at the Fairmont Hotel, San Francisco, California on Saturday evening, June 19, Dr. David Salkin, San Fernando, California, chairman of the Committee on College Essay, announced the following winners of the 1954 prize essay contests:

First Places (tie):

Lionel H. Opie, Cape Town, South Africa
"The Pulmonary Manifestations of Generalized Scleroderma (Progressive Systemic Sclerosis)."

Arnold Victor, New York, New York
"The Early Diagnosis of Primary Lung Cancer."

Second Place:

Ian N. Lee, London, England
"Pulmonary Metastases."

Third Place:

J. C. Jacob, Vellore, South India
"Chemical Burns and Corrosive Stricture of the Esophagus."

As the committee had concluded that there was a tie for first place, two prizes of $250.00 and two certificates of first prize were awarded. The committee recommended that in the future contests three monetary prizes be offered, namely, $250.00 for first place, $100.00 for second place, and $50.00 for third place. This recommendation was approved by the Board of Regents at its annual meeting and will take effect in the 1955 Essay Contest. The Board of Regents recommended that members of the College affiliated with medical schools be urged to bring the contest to the attention of the student body at their respective schools. The Essay Contest is open to undergraduate medical students throughout the world and the essays may be written on any phase of cardiac or pulmonary disease.

Committee on Scientific Program

Physicians who wish to present papers in the scientific assembly of the 21st Annual Meeting of the American College of Chest Physicians, to be held in Atlantic City, New Jersey, June 5-8, 1955, are invited to send their titles and brief abstracts of their papers to Dr. Burgess L. Gordon, Women's Medical College, Philadelphia, Pennsylvania, the Chairman of the Committee on Scientific Program. Other members of the Committee are: Alvan L. Barach, New York City; John F. Briggs, St. Paul, Minnesota; Sumner S. Cohen, Oak Terrace, Minnesota; and Alfred Goldman, Los Angeles, California.

Motion Picture Session on Diseases of the Chest

Physicians having new motion pictures on diseases of the chest are invited to send their films for review by the Committee on Audiovisual Aids of the American College of Chest Physicians for official approval and for consideration for showing at the 1955 annual motion picture session to be held in connection with the 21st Annual Meeting of the College in Atlantic City, June 2-5, 1955. Film data blanks may be had upon request. Please address films and inquiries to Dr. Paul H. Holinger, Chairman, Committee on Audiovisual Aids, American College of Chest Physicians, 112 East Chestnut Street, Chicago, Illinois. Other members of the committee are: Houck E. Bolton, Philadelphia, Pennsylvania; Alfred Goldman, Los Angeles, California; H. Corwin Hinshaw, San Francisco, California; David H. Waterman, Knoxville, Tennessee; and Francis M. Woods, Brookline, Massachusetts.

Third International Congress on Diseases of the Chest

The scientific program to be presented at the Third International Congress on Diseases of the Chest, Barcelona, Spain, October 4-8, was published in the August issue of *Diseases of the Chest*. In addition, there will be a panel discussion at the close of each day's scientific sessions on Tuesday, Wednesday, Thursday and Friday, October 5 through 8. The following moderators and participants have accepted invitations to serve on these panels:

Tuesday, October 5 — "Tuberculosis"

Richard R. Trail, *Moderator*, London, England
Donato G. Alarcon, Mexico City, Mexico
Etienne Bernard, Paris, France
Emil Bogen, Olive View, California, USA
Alfred F. Brunner, Zurich, Switzerland
Jorgen Lehmann, Gothenburg, Sweden
Rolf Griesbach, Augsburg, Germany
Gumersindo Sayago, Cordoba, Argentina
A. Omodei Zorini, Rome, Italy

Wednesday, October 6 — "Asthma and Emphysema"

Andrew L. Banyai, *Moderator*, Milwaukee, Wisconsin, USA
Ovidio Garcia Rosell, Lima, Peru
H. N. Knipping, Cologne, Germany
Wilhelm Loeffler, Zurich, Switzerland
Arthur M. Olsen, Rochester, Minnesota, USA
Harry L. Rogers, Philadelphia, Pennsylvania, USA
Raul F. Vaccarezza, Buenos Aires, Argentina

Thursday, October 7 — "Cardiovascular Disease"

John F. Briggs, *Moderator*, St. Paul, Minnesota, USA
Clarence Crafoord, Stockholm, Sweden
L. D. Eerland, Groningen, The Netherlands
James Alexander Lyon, Washington, D. C., USA
Olivier Monod, Paris, France
Antonio Rodriguez-Diaz, Havana, Cuba
Arsenio Cordeiro, Lisbon, Portugal
Ray W. Kissane, Columbus, Ohio, USA

Friday, October 8 — "Tumors of the Chest"

Chevalier L. Jackson, *Moderator*, Philadelphia, Pennsylvania, USA
Anthony Caralps, Barcelona, Spain
Manoel de Abreu, Rio de Janeiro, Brazil
Seymour M. Farber, San Francisco, California, USA
Andre Meyer, Paris, France
Richard H. Overholt, Brookline, Massachusetts, USA
J. Swierenga, Utrecht, The Netherlands
Hans Wurm, Wiesbaden, Germany

A special room will be set aside for the presentation of current motion picture films on all aspects of diseases of the chest.

College Chapter News

KENTUCKY CHAPTER

The annual luncheon and business meeting of the Kentucky Chapter will be held September 21 at the Brown Hotel in Louisville. Guest speaker will be Dr. Thomas J. E. O'Neill of Philadelphia. The chapter will also present a Specialty Group Scientific Meeting in conjunction with the annual meeting of the state medical association on September 22 at the Columbia Auditorium at which the following program will be presented:

"Common Clinical Problems of Fungus Disease,"
Daniel N. Pickar, Louisville, Kentucky.

"The Surgery of Stenotic Valvular Disease—Indications and Results,"
Thomas J. E. O'Neill, Philadelphia, Pennsylvania.

"Home and Office Treatment of Pulmonary Tuberculosis,"
D. G. Miller, Jr., Morgantown, West Virginia.

"Sanatorium Care of Tuberculosis,"
J. Frank W. Stewart, Waverly Hills, Kentucky.

NORTH CAROLINA CHAPTER

The Fifth Annual Meeting of the North Carolina Chapter will take place at the Robert E. Lee Hotel, Winston-Salem, October 16. Dr. Ralph E. Moyer, Oteen, chapter President, will preside over the scientific session beginning at 1:30 p.m. The following program will be presented:

"Recent Trends in the Surgery of Tuberculosis,"
J. D. Murphy, Oteen.
Discussor: Richard T. Myers, Winston-Salem.

"Clinical Pathological Conference,"
Officers and Staff of the Medical and Surgical Service, Veterans Administration Hospital, Oteen.

"X-ray Conference" (Panel Discussion),
J. P. Rousseau, Winston-Salem; Kenneth V. Tyner, Winston-Salem; M. D. Bonner, Jamestown; and Norman L. Anderson, Asheville.

Business Session.

Dinner — 6:00 P.M.

Evening Session — 8:00 P.M.
Guest Speaker: Francis M. Woods, Brookline, Massachusetts,
"Varied X-ray Manifestations of Bronchogenic Carcinoma."

ROCKY MOUNTAIN CHAPTER

The Rocky Mountain Chapter, which includes the states of Colorado, New Mexico, Utah, and Wyoming, will hold its annual meeting September 25, at the Broadmoor Hotel, Colorado Springs, Colorado, in conjunction with the meeting of the state medical association. The following program will be presented:

9:00 a.m. — Registration.

"The Pathology of the Resected Lung with Isoniazid Therapy,"
John H. Denst, Denver, Colorado.

"Osteoarthropathy in Pulmonary Lesions,"
William Wierman, Denver, Colorado.

"Chronic Pneumonia,"
H. W. Harris, Captain, MC, Denver, Colorado.

"Reaction of Serous Membranes to Blood,"
John S. Chapman, Dallas, Texas.

12:00 Noon — Luncheon meeting and Panel Discussion:
"When Not to do Lung Resections for Pulmonary Tuberculosis,"
H. M. Van Der Schouw, Wheat Ridge, *Moderator*.

Fred R. Harper, Denver; Robert Brown, Denver; John S. Chapman, Dallas; Albert H. Andrews, Jr., Chicago; and John H. Denst, Denver.

2:00 p.m. — "Therapeutic Diagnosis in Obstructive Emphysema,"
Albert H. Andrews, Jr., Chicago.

"Constrictive Pericarditis,"
Edwin Goyette, Colonel, MC, Denver.

"A Review of the Methods Used in Hay Fever Therapy,"
B. T. McMahon, Denver.

POTOMAC AND VIRGINIA CHAPTERS

The annual meetings of the Potomac and Virginia Chapters will be held jointly in Washington, D. C., on October 31 at the Shoreham Hotel, immediately preceding the joint meeting of the Virginia and District of Columbia Medical Societies, November 1-3. The following program has been arranged by the Committee on Scientific Program under the Chairmanship of Dr. Roy G. Klepser, Washington, D. C.:

10:00 a.m. — *Symposium: "Cardiac Surgery,"*
Edgar W. Davis, Washington, D. C., *Moderator*.

"Interatrial Septal Defects," Elton Watkins, Boston, Massachusetts.

"Surgery of the Aorta," Henry T. Bahnson, Baltimore, Maryland.

"Plastic Valves in Aortic Insufficiency," Charles A. Hufnagel, Washington, D.C.

12:30 p.m. — *Round Table Luncheons,*

A. "Pulmonary Emphysema,"
James J. Feffer, Washington, D. C., *Moderator*.

Bruce Armstrong, Baltimore, Maryland; Milton Gusack and Paul Jacquet, Washington, D. C.

B. "Evaluation of Patients for Cardiac Surgery,"
Bernard J. Walsh, Washington, D. C., *Moderator*.

John O. Nestor, Washington, D. C. and Robert P. Glover, Philadelphia, Pennsylvania.

2:00 p.m. — *Panel Discussion:*
"Problems Encountered in the Present Day Management of Tuberculosis,"
Sol Katz, Washington, D. C., *Moderator*.

"Chemotherapy," Moe Weiss, Glenn Dale, Maryland.

"Medical Problems," Edward S. Ray, Richmond, Virginia.

"Out-Patient Clinics," Donald R. Sickler, Washington, D. C.

"Surgical Management," Everett C. Drash, Charlottesville, Virginia.

Symposium: "Bronchogenic Carcinoma,"
Frank S. Ashburn, Washington, D. C., *Moderator*.

"Epidemiologic Research," Harold Dorn, Bethesda, Maryland.

"Pathology, Gross and Microscopic," Harold L. Stewart, Bethesda, Maryland.

"Exfoliative Cytology," Albert W. Hilberg, Bethesda, Maryland.

"Surgical Outlook," M. Lawrence White, Huntington, West Virginia.

"Medical Therapy, X-ray vs. Drugs," Louis K. Alpert, Washington, D. C.

Discussion.

5:00 p.m. — Business meeting, Potomac Chapter.
Business meeting, Virginia Chapter.

WISCONSIN CHAPTER

The Wisconsin Chapter will hold its annual meeting at the Schroeder Hotel, Milwaukee, October 3. After a business meeting and luncheon, the following papers will be presented:

2:00 p.m. — "The Differential Diagnosis of Carcinoma of the Lung,"
Herman J. Moersch, Rochester, Minnesota.

"Management of Cardiac Emergencies,"
Howard L. Correll, Milwaukee.

"Recent Advances in Inhalation Therapy in Bronchopulmonary Diseases,"
Edwin R. Levine, Chicago, Illinois.

"Benign Tumors of the Chest,"
William M. Lees, Chicago, Illinois.

"Clinical Aspects of Hypertension of the Greater and Lesser Circulation,"
Charles W. Crumpton, Madison.

A number of interesting scientific exhibits on chest diseases will be shown in connection with the meeting.

1955 COLLEGE DIRECTORY

Forms for a listing in the 1955 Directory of the American College of Chest Physicians have been mailed to all members of record. To assure a correct listing in the new Directory, it is essential that members return their forms promptly. Members who have not received Directory forms, please notify the Executive Director, American Colege of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois, U.S.A. at once. Members are given the opportunity to purchase a copy of the Directory at the pre-publication price of $5.00. After publication the Directory will be priced at $7.50 per copy.

The American College of Physicians will sponsor the first nation-wide closed circuit television broadcast for postgraduate medical education on September 23 from 6:00 to 7:00 p.m. Eastern Daylight Saving Time over the Columbia Broadcasting System. The program, a Symposium on the Management of Hypertension, cannot be viewed in the home, but the invited audience may go to the TV receiving stations in the following cities: Boston, New York, Philadelphia, Washington, Pittsburgh, Charlotte, Atlanta, Cincinnati, Detroit, Chicago, St. Louis, Milwaukee, Minneapolis, Memphis, Dallas, Houston, New Orleans, Denver, Salt Lake City, Los Angeles, San Francisco, Baltimore, and Cleveland. Panel members will be Doctors Cyrus C. Sturgis, F. H. Smirk, Garfield G. Duncan, R. W. Wilkins, and Edward D. Freis.

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Obituary

LOUIS MARK

1892 - 1954

Louis Mark was born at Duluth, Minnesota, on December 11, 1892. After graduating from Ironwood, Michigan, Hich School, he entered Marquette University in Milwaukee and received the degree of Doctor of Medicine in 1915. His internship was served at Cincinnati General Hospital, where he became especially interested in diseases of the chest on the service of the famous Kennon Dunham in the Tuberculosis Branch Hospital now known as Dunham Hospital. He then entered private practice at Washburn, Wisconsin. In 1918 he was resident physician at Ohio State Sanatorium, and one year later he purchased Rocky Glen Sanatorium at McConnelsville, Ohio. After organizing this institution to his complete satisfaction he moved to Columbus, Ohio, where he constructed the Mark Building in which he established offices for the practice of diseases of the chest. Throughout the years he spent one day each week at Rocky Glen Sanatorium, keeping in close touch with the patients and directing the activities of the staff. For many years he was also medical director of the Jane M. Case Tuberculosis Hospital at Delaware, Ohio, where he spent one-half day each week.

In 1921 Dr. Mark was appointed attending specialist in tuberculosis, United States Veterans Bureau, and served in this capacity for many years. He had long been chief of the chest department of White Cross Hospital in Columbus. He was tuberculosis advisor for the Brotherhood of Railroad Trainmen for over 30 years. He also helped guide the chest program of the United Mineworkers' Welfare and Retirement Fund from its inception.

Throughout the years, Louis Mark remained in the forefront by gaining and retaining the best knowledge of the time on the diagnosis, treatment, and prevention of diseases of the chest. He took postgraduate work in a number of American universities and hospitals, in addition to reading various local, national and international medical journals, which enabled him to provide his patients with most modern medicine. In the later years of his life he was so well and favorably known that he was invited to lecture, not only throughout the United States, but in numerous other countries, including England, France, Greece, Italy, Israel, Spain, and many South and Central American nations. While in Rome in 1950 he had a long private interview with Pope Pius XII, which he cherished through his remaining years. He was never too busy to assist other physicians, whether they be in the general practice of medicine or expert in diseases of the chest.

He was in demand in medical organizations and held membership in the Columbus Academy of Medicine, the Ohio and American Medical Associations,

and the American College of Physicians. He was also a member of the American Physicians Fellowship Committee of the Israel Medical Association. He was a founder of the American College of Chest Physicians, was president of the Ohio chapter and president of the College in 1950. That year he presided over the First International Congress on Diseases of the Chest in Rome. Dr. Mark served as the Chairman of the Committee which negotiated the purchase of the College Building in Chicago.

In addition to conducting a large private practice and directing the work in diseases of the chest in three hospitals, he traveled more than 700,000 miles, covering every state of this nation, each province of Canada, Central and South America, and Europe. His travels began in 1920 with 15,000 miles, and increased to 35,000 miles a year since 1945.

He became an expert photographer and had a collection of 5,000 still pictures and some 20,000 feet of motion picture films from various parts of the world.

While Louis Mark was a student at Marquette University he played on the football team, where as the smallest member of the squad he won the reputation of a good and clean fighter. His interest in sports and games continued throughout life. He was a fine two-handicap golf player, having been champion of the Winding Hollow Club at Columbus for 17 years. He was third in the American Medical tourney, second twice, and third three times in the Ohio State Medical tournament. He won approximately 100 golf trophies.

As a bridge player, Dr. Mark was the first physician in the nation to become a Life Master. He aided in organizing the Central Ohio Bridge League and in 1948 and 1949 was president of the American Contract Bridge Association. He was a member of its board and thus aided in shaping its policies. His bridge trophies, local, state, and national, numbered more than 200, and included the president's in the National tournament won in 1938.

Louis Mark had a splendid philosophy of life. He said, "The secret of living is being able to see the other fellow's side of things, whether he be an employee, a patient, a friend, or someone who doesn't like you. And one other thing is being able to have a little fun."

At the age of 60, he said, "Life has been good to me, but life is only what you make it. Many people don't learn to give, only to take. You have to give yourself and your money to enjoy life. Whatever you do—do it wholeheartedly."

On October 7, 1919, Louis Mark was married to Fanny Karon of Duluth, Minnesota. This most devoted couple was almost inseparable over the next 35 years, till death. Mrs. Mark's interest in all of his activities and her undaunted encouragement in his undertakings contributed mightily to his success and happiness. She accompanied Louis on practically all of his journeys throughout North America and numerous other nations. Moreover, she participated in all of his major decisions.

Their extensive travels with photographic records, together with their unsurpassed geniality and their unqualified respect of all people regardless of race, nationality and religion, enabled them to win and retain hosts of friends everywhere. In attending local, national and international conventions, Louis and Fanny Mark practically always arranged for one or more occasions in their hotel suite, consisting of most wholesome entertainment for their friends. It is doubtful if anyone was ever able to reciprocate adequately.

They reared three children, now Mrs. Charlotte Mentser, Mrs. Louise Levitin of Columbus, and Dr. Lloyd Mark, Boston City and Children's Hospital, Boston. They also have six grandchildren.

Dr. Mark was well known in Columbus for his charitable and social gifts of both time and money. He was a member of the Athletic Club, Excelsior Club, Chamber of Commerce, Scottish Rite, Masons, Big Brothers' Association, and an honorary Rotarian. He was a successful financier. Through long hours of work each day,

a methodical saving plan, good investment judgment, a sense of honesty that deserved confidence everywhere, his financial successes far surpassed those of most physicians. In this accomplishment he had an honorable record of having given value received for everything he possessed. He was so trusted by acquaintances, friends and organizations that his advice was often sought in their financial affairs.

He could always adapt with good grace and understanding to changing situations. Only a few months ago, in a personal conversation he pointed out to me that the Rocky Glen Sanatorium, the largest private institution of its kind in the country, had provided treatment and care for a large number of persons since 1919 and was continuing to do so. However, he stated that with the rapid decrease in the incidence of tuberculosis, the great number of additional beds being provided by state and county institutions in Ohio and other states, there would not much longer be need for his sanatorium. Nevertheless, he was desirous of having it continue to serve humanity. Therefore, he was thinking of gradually converting it to an institution for nontuberculous elderly people, of whom there are so many in dire need of such care.

One rarely meets an individual with such versatility and spontaneity as Louis Mark possessed. When called upon without previous notice on almost any occasion, he could speak to the point, always to the enlightenment and satisfaction of his audience. To him, time was always of the essence. He never bored or embarrassed individuals or audiences with long, empty conversations and addresses.

He was calm, but generous to a fault. There was nothing in his power that he would not do to support and aid a friend or a worthy person in need. He was devoted to his patients and thus did everything that was humanly possible for them. There are literally thousands of persons living today whom he aided in the restoration of health.

The last paper he published, entitled "Loeffler's Syndrome," appeared in February, 1954. This paper contained ingenious methods which he had found satisfactory in treating this condition. During a recent personal conversation he told me of his plan to analyze large volumes of data on various diseases of the chest which he had assembled throughout his long professional career. At that time he had slight manifestations of ill health which were later proved to be due to malignancy. He was admitted to the White Cross Hospital in Columbus, where, after four weeks he died, on February 25, 1954. Immediately following Dr. Mark's death, the following statement appeared in the *Columbus Citizen:* "He leaves behind him a record of years so full of good deeds, accomplishments, interests, charities, and travels marked by such a driving energy and deep honesty that they should inspire others to fill their empty lives."

With his life something went out of his city, his state, and the world which will never return, but much remains. His kindly spirit, sincerity of purpose, loyalty to friends and contributions to knowledge have become a part of thousands now living who will pass them on to succeeding generations.

J. ARTHUR MYERS.

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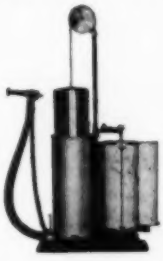

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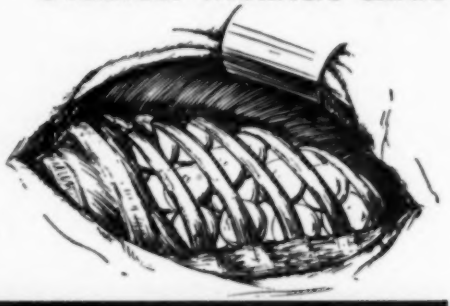

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NATIONAL AND INTERNATIONAL MEETINGS

Third International Congress on Diseases of the Chest
Council on International Affairs
American College of Chest Physicians
Barcelona, Spain, October 4-8, 1954.

Interim Session American College of Chest Physicians
Delano Hotel, Miami Beach, Florida, November 28-29, 1954.

POSTGRADUATE COURSES

9th Annual Postgraduate Course on Diseases of the Chest
Hotel Knickerbocker, Chicago, Illinois, October 18-22, 1954.

Postgraduate Course on Diseases of the Chest
Bunts Institute, Cleveland, Ohio, October 27-28, 1954.

7th Annual Postgraduate Course on Diseases of the Chest
Hotel New Yorker, New York City, November 8-12, 1954.

CHAPTER MEETINGS

Kentucky Chapter, Louisville, September 21-22, 1954.

Rocky Mountain Chapter, Colorado Springs, Colorado, September 25, 1954.

Wisconsin Chapter, Milwaukee, October 3, 1954.

North Carolina Chapter, Winston-Salem, October 16, 1954.

Potomac and Virginia Chapters (Joint Meeting),
Washington, D. C., October 31, 1954.

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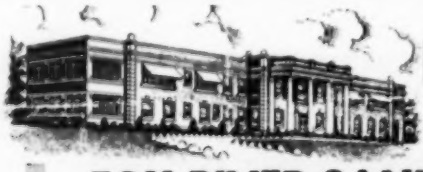

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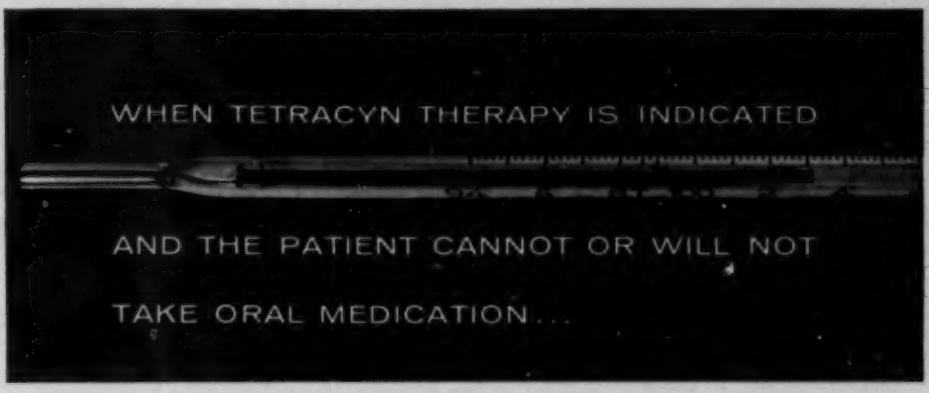

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